The New England
Journal of Medicine

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Volume 254 APRIL 12, 1956 Number 15

ADDUCTION CONTRACTURE OF THE THUMB*

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BOSTON

ADDUCTION contracture of the thumb presents a most serious disability of the hand. The thumb is useless as an opponent for the fingers, is unable to abduct and rotate and, in some cases, blocks flexion of the fingers. The hand is incapable of proper grasp, pinch and stereognosis. The proper mechanics of position of the thumb are crippled.

A B

FIGURE 1. *Adduction Contracture of the Right Thumb in Case 1* (A), *with Opposition Restored after Excision of Scar and Skin Grafting* (B).

*Presented at the tenth annual meeting of the American Society for Surgery of the Hand, Los Angeles, California, January 28, 1955.

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FUNCTIONAL ANATOMY

The thumb is controlled by 4 long and 6 short muscles arranged about its circumference and supplied by the radial, median and ulnar nerves. Roughly, the radial controls extension, the median flexion, and the ulnar adduction. No one muscle acts alone, and all motions are the results of co-ordinated action of all muscles. Thus, the motion in one joint usually requires fixation in appropriate position of the joints proximal to the one being moved. Also, whenever any muscle contracts there must be a reciprocal re-

laxation of its opponent. The complexity of integrated thumb motion can be easily appreciated.

The thumb motions are flexion, extension, abduction, adduction, circumduction, opposition, rotation and apposition. All motions are customarily described as though the patient were erect, the arm at his side, the forearm supinated, the wrist halfway between flexion and extension, and the fingers extended.

Flexion and extension require no further explanation except that as part of extension, the thumb is pressed forcibly against the radial border of the hand.

Abduction moves the thumb away from the radial border of the hand and holds the thenar eminence so that it cannot slip forward and ulnarward into the palm.

When the thumb is adducted it moves strongly against the radial side of the hand and across and in front of the radial third of the palm. In addition the first metacarpal bone moves ulnarward, swinging in that direction from a pivot at the carpometacarpal joint.

In circumduction the thumb swings in a circle with the metacarpophalangeal joint as the center.

Opposition, the most complicated and least clearly understood of all the thumb motions, is carried out in a plane forward of the plane of the palm and the volar surfaces of the fingers, and precludes contact at any point between the thumb and the palm or fingers. In opposing the thumb, the thumb nail, which normally and in adduction remains with its broad axis at right angles to the plane of the palm, is so altered in position that its broad axis becomes parallel to and in front of the plane of the palm in opposition. This is accomplished by a rotation of the thumb on its own axis through an arc of 90°; this motion is a component part of the movement of the thenar eminence forward, ulnarward and into the front of the radial third of the palm.

Apposition is accomplished after opposition and involves added flexion of the terminal phalanx of the thumb as well as flexion of either the distal or the last two phalanges of the fingers.

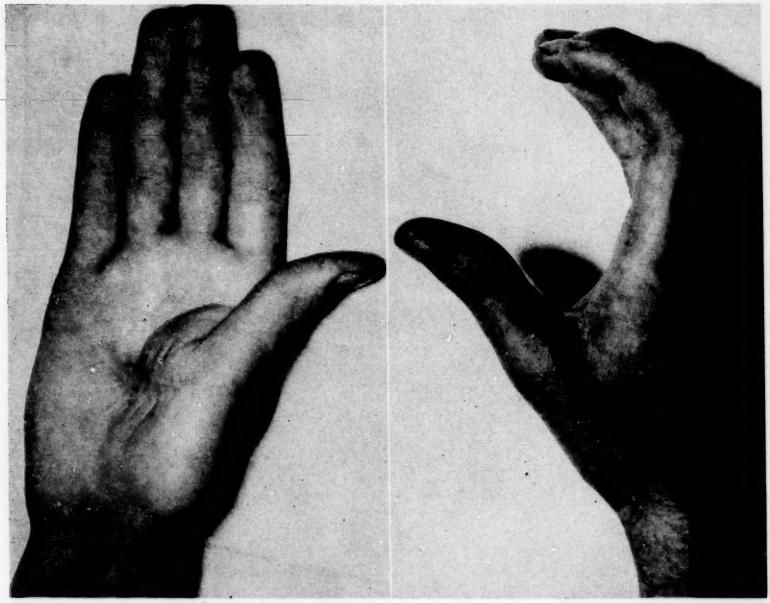

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FIGURE 2. *Adduction Contracture Due to Laceration and Resultant Scar in Case 2* (A), *with Abduction and Opposition after Excision of Scar and Skin Grafting* (B).

Adduction Deformity

Adduction deformity in its simplest form predicates fixation of the thumb in the position of adduction against the radial border or in front of the radial plane of the palm. Extension of the thumb, in the usual sense, is impossible and, when attempted, serves only to adduct the thumb even more strongly. The pathology in such a case includes scar contraction,

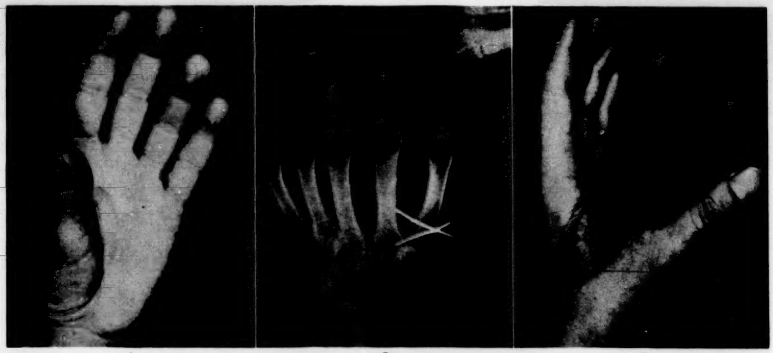

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FIGURE 3. *Adduction Contracture Due to Buffing — Machine Injury in Case 3* (A), *Treated by Crossed Kirchner Wires to Maintain the Proper Relation between the First and Second Metacarpal Bones* (B), *with Satisfactory Abduction and Opposition after Operation* (C).

third of the palm of the hand. Use of the hand is lost because apposition and opposition are lost, and full flexion of the index and long fingers is prevented by the presence of the thumb in front of their normal resting places. The simplest cause of this loss of function is a contracted scar of the skin of the thenar web. At the other extreme and in its most complicated form the thumb is flexed at its terminal interphalangeal joint and fixed against and in front of the palm so as virtually to cover all the palm, the thenar eminence is pulled ulnarward and forward and fixed in this position, and rotation of the thumb on its own axis is impossible. As a result the thumb nail in this fixed position is still at right angles to the atrophy and destruction of the involved intrinsic muscles, possible fractures, extensive skin destruction and contraction, the movement and subsequent fixation of the distal end of the first metacarpal bone backward and ulnarward against the second metacarpal, an adherent sheath of the extensor pollicus longus tendon and involvement of the palmar fascia by destruction and scarring.

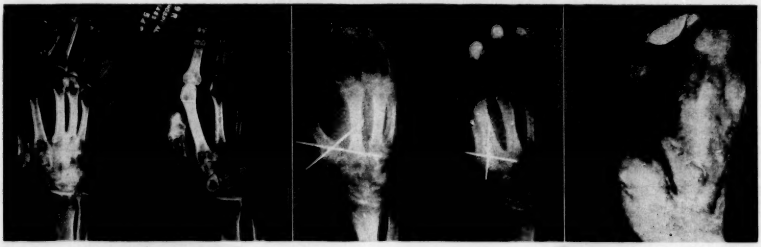

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FIGURE 4. *Adduction Contracture after a Mangle Injury in Case 4* (A) *Corrected by Operation, the Proper Relation between the First and Second Metacarpal Bones Being Maintained by Crossed Kirchner Wires, with Increased Opposition* (B) — *to Be Further Increased by Osteotomy.*

Between these two extremes the surgeon will find all varieties of combination, but, in general, the deformity will be such as to preclude opposition, apposition, adequate flexion of the index and long fingers and maximal loss of effective function of the hand.

Etiology

The commonest causes of adduction contracture of the thumb are burns, trauma, infection, ischemia, paralysis, spastic conditions and improper splinting. The burns may be thermal, chemical or electric. With trauma, the wounds may be crushed, avulsed and incised, especially those caused by gunshot. Infections of the thenar space, the tendon sheaths of the thumb, index and middle fingers and the first lumbrical space have resulted in adduction contracture.[1]

Ischemia of the hand may also be a cause. This ischemia is most often due to swelling of the hand when it is encased in plaster or wrapped in too tight an elastic bandage. The contracture may also follow gross damage to large blood vessels and nerves in the arm.[2]

The resultant paralysis, because of the unopposed pull of the antagonists, may be a cause. This is especially true in spastic patients. Among this group the cerebral palsies are the most difficult to treat.[3] Associated improper splinting in the treatment of this condition or fractures is a common cause and in many cases, particularly those of fracture, avoidable by proper splinting of the thumb in opposition.

Treatment

Therapeutic requirements are based on and their success measured by the ability of the surgeon to reproduce the normal anatomic relation that existed before the injury. These requirements vary with the severity and extent of the injury. Therapy starts with methods designed to prevent the development of deformities and loss of function and, as such, cannot be applied too soon after the accident. Of all such immediately applicable methods proper splinting is the most important. The whole hand, especially the thumb, must be splinted in the position of function based on stabilizing splints to which, if necessary, traction can be added. Of course, proper general and local surgical therapy must also be used as required. Blood transfusions, hospitalization, attention to fluid and electrolyte needs, local dressings and débridement as indicated should be stressed. It is well, too, for the surgeon to permit antibiotics and similar drugs to be included only as adjuvants to the basic surgical therapy and not to give them first place and thus neglect the other tried and true methods of treatment.

If these primary therapeutic requirements have been neglected or carried out ineffectively and contractures, deformities and limitation or loss of function have developed, the surgeon has a more complicated and difficult problem to deal with.

Such a later condition, together with its treatment, results and prognosis, forms the subject of this communication. The object of the therapy of deformed hands is to restore normal elasticity to the skin, correct fascial, scar and muscular contractions, release tendon-sheath adhesions and replace the mis-

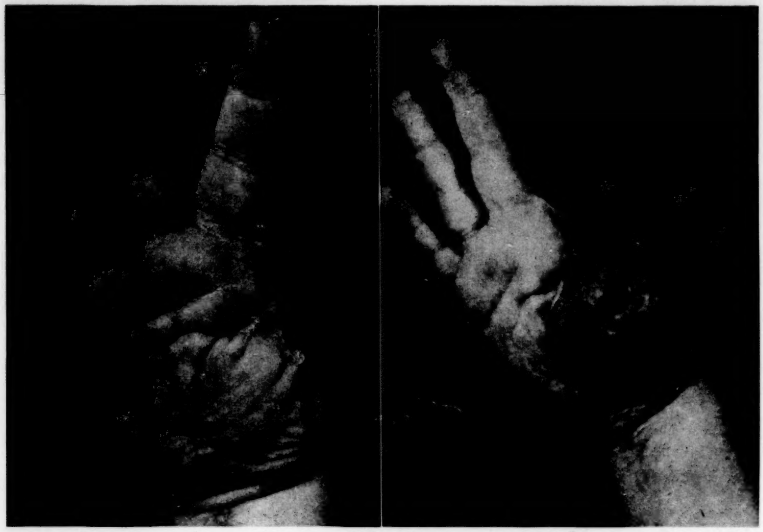
A B

Figure 5. *Severe Adduction Contracture as a Result of a Press Injury in Case 5* (A), *with Satisfactory Opposition and Grasp* (B) *after Excision and Skin Grafting.*

placed first metacarpal bone in its proper normal relation to the second metacarpal and the proximal end of the first thumb phalanx. Depending on the success attained, flexion, extension, abduction, adduction, opposition, apposition and rotation of the thumb will be restored in varying degree.

The majority of cases must be corrected by operation. Simple skin contractures may be relieved by Z-plasty. With extensive skin contractures after burns and trauma, the scar is excised and a full-thickness or thick intermediate-thickness graft is applied. In some cases of deep electric burns or paralysis, the skin is adequate, and a division of the insertion of the adductor pollicis alone will permit full passive mobility of the thumb.

In most cases the skin and deep structures are contracted, and the necessary operation is more extensive, the incision being carried through the center of the thenar web, from volar to dorsal apex. The insertion of the adductor pollicis muscles is incised. All contracting tissues are excised. Usually, the first dorsal interosseous muscle and a part of the palmar fascia are involved. Opposition and the proper V relation of the first two metacarpal bones is maintained by two crossed Kirchner wires inserted into the first and second metacarpals. Permanent fixation, in opposition, may be used when mobility is not gained or maintained by the wires by means of a bone strut or by fusion of the carpometacarpal joint. A pedicle graft, from the abdomen, is used to cover the skin defect. This graft has usually been constructed previously as a rope. A diamond pattern of pedicle at the donor site gives a graft that later forms a good web, has good palmar and dorsal surfaces and, when in place on the hand, eliminates any suture line between the metacarpal heads.



A B

FIGURE 6. *Adduction Contracture of the First Metacarpal after a Lawn-Mower Injury in Case 6* (A), *with Fair Pinch and Grasp Ability* (B) *after Abdominal-Tube Skin Graft. The recent graft will be defatted later.*

In some cases after the contracted muscles have been excised, the mobilized thumb must be reactivated by tendon transfer to compensate for the intrinsic muscle loss. Transfer of the opponens is the commonest procedure. In such cases some degree of splinting is maintained after the period of immobilization and until the transferred tendon has gained enough power and amplitude to maintain the thumb in a functional position.

An adherent extensor pollicis longus tendon may have to be displaced from its scarred sheath into the soft subcutaneous tissue.

For practical purposes the thumb has to be placed so that the tips of the index and middle fingers can converge against the pulp of the thumb.

Case Reports

The following cases serve as examples of the various extents of adductor contractures, the different causes and the various procedures that have been adopted to correct them.

Skin Contracture

In 2 cases deformity developed because of skin contracture only — 1 as the result of burns, and the other as the result of trauma. Both were corrected by excision of the scar and skin grafting.

Case 1. An 11-year-old boy was severely burned when a kerosene lamp exploded. Both arms and hands, both thighs and abdomen had 2d-degree and 3d-degree burns. An adduction contracture of the right thumb developed (Fig. 1*A*).

At operation, when the scarred skin was excised from the web, the thumb could easily be placed in the position of opposition. A thick split-thickness graft was sutured to the skin defect. Dressings were applied for 2 weeks, and then active exercises were begun. Normal abduction and opposition of the right thumb were obtained (Fig. 1*B*).

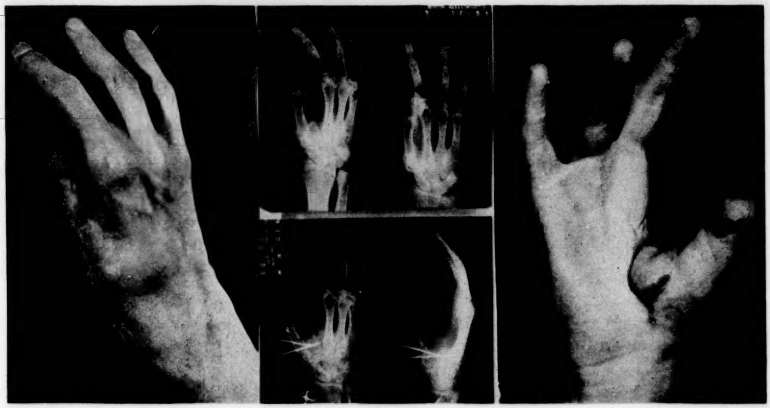
Case 2. An 18-year-old boy had received a laceration of the palm of the right hand on a broken bottle 12 years previously. Adduction contracture of the right thumb from the skin cicatrix gradually developed (Fig. 2*A*).

At operation, the skin scar was excised, the thumb placed in the position of opposition, and a full-thickness skin graft cut from the thigh and sutured to the defect on the hand. Normal opposition and abduction of the thumb resulted (Fig. 2*B*).

Deep Contractures Due to Trauma

There were 3 cases of deep adduction contracture that were due to trauma. In each case the trauma was crushing in type, being caused by a buffing machine, a mangle and a press. In each the adduction contracture was preceded by various and multiple operations and involved the skin, the adductor pollicis muscle, the first dorsal interosseous muscle and the palmar fascia.

Case 3. A 25-year-old woman received a crushing injury to the left thumb and left hand by a buffing machine. There was a fracture of the proximal phalanx of the left thumb. Four operations (1 a full-thickness skin graft) had been performed. Physical examination showed an adduction contracture of the left thumb. A full-thickness skin graft measuring 3 by 2 cm. had been placed over the volar aspect of the left thumb. There was shocklike tenderness over the medial and lateral scars (Fig. 3*A*).



A B C

Figure 7. *Severe Adduction Contracture after a War Injury in Case 7* (A), *Showing Satisfactory Relation between the First and Second Metacarpal Bones Maintained by Crossed Kirchner Wires* (B) *and Satisfactory Opposition after Operation* (C).

An abdominal-tube skin graft was constructed. To correct the adductor contracture, the insertion of the adductor pollicis was incised, and the 1st dorsal interosseous muscle, as well as a part of the palmar aponeurosis, was excised. Two crossed Kirchner wires, through the 1st and 2d metacarpals, maintained the proper relation of these bones (Fig. 3*B*). The skin defect was covered with the abdominal-tube graft. Fair opposition and good abduction resulted (Fig. 3*C*). There was also some active rotation of the thumb, after removal of the wires in 9 weeks.

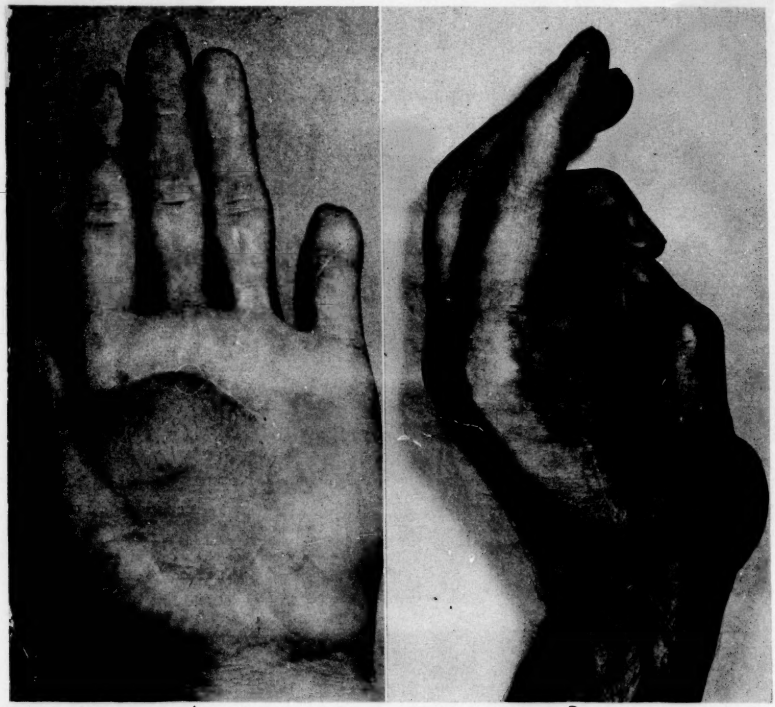
Case 4. A 23-year-old coastguardman received severe crushing injuries to his right hand in a mangle. Four operations, 2 of which were skin grafts, resulted in stiffness of all the fingers, with active motion of only 5° in all metacarpophalangeal joints and 20° in each distal interphalangeal joint. The right thumb had been amputated at the neck of the proximal phalanx, and there was a pronounced adduction contracture of the remnant of the thumb.

An abdominal-tube skin graft was taken. The adductor pollicis and 1st dorsal interosseous muscles were excised, and a partial excision of the palmar aponeurosis was performed. The thumb was maintained in proper relation by crossed Kirchner wires put through the 1st and 2d metacarpals (Fig. 4*A*). The tube graft covered the skin defect. Fair opposition resulted (Fig. 4*B*).

CASE 5. A 30-year-old man received a crushing injury to the right hand between 2 rolls of a press. There had been 3 operations, 2 of which were skin grafts. Stiffness of all fingers resulted, with a flexion deformity of 70° in the metacarpophalangeal joints that was due mainly to a palmar scar. The right thumb had been amputated through the base of the proximal phalanx. The 1st metacarpal was adducted (Fig. 5*A*).

An abdominal-tube skin graft was constructed. The palmar scar, palmar aponeurosis, adductor pollicis muscle and 1st dorsal interosseous muscle were all excised. Two crossed Kirchner wires, put through the 1st and 2d metacarpals, maintained their proper relations. The skin defect of the palm and thumb-index web was covered by the detached pedicle skin graft. Good pinching ability between the thumb stump and the tips of the index, middle and ring fingers resulted (Fig. 5*B*).

A tube skin graft was constructed on the abdomen. To correct the adductor contracture, a cleft was deliberately formed between the 1st and 3d metacarpals. The adductor pollicis was incised near its attachment, and the 1st and 2d dorsal interosseous muscles and part of the palmar fascia were excised. The 1st volar interosseous muscle was cut. Two crossed Kirchner wires provided satisfactory relation between the 1st and 3d metacarpal bones. The tube skin graft was sutured to the skin defect overlying the cleft. Fair ability to pinch and grasp resulted (Fig. 6*B*).



A B

FIGURE 8. *Adduction Contracture after a Battle Injury in Case 8* (A), *with Opposition after Operation* (B).

Contracture after Avulsion and Ischemia

CASE 6. A 3-year-old boy received extensive avulsed wounds of the right hand when he caught it in a power lawn mower. Two operations had been performed, the later being an amputation of the right thumb, index finger and 2d metacarpal bone because of ischemic gangrene. The 1st metacarpal bone became adducted in the process of wound closure by skin grafting (Fig. 6*A*).

Adduction Contracture after War Injuries

CASE 7. A 26-year-old infantryman received a gunshot wound of the right forearm in combat in Korea. There was a fracture of the right radius, and division of the median, ulnar and radial nerves. Gangrene of the right index finger and the tip of the right thumb developed. Seven operations were performed, including a ligation of the right radial artery, a dorsal sympathectomy, an intermediate-thickness skin graft of the right forearm, a pedicle skin graft of the right thumb, an amputation of the right index finger, reconstruction of the thumb-index web and an excision of the scar from the right forearm.

Three years after the injury, when the patient was first seen at the Boston Veterans Administration Hospital, it was found that the right index finger had been amputated through the proximal ⅓ of the 2d metacarpal, and the

thumb through the neck of the proximal phalanx, after which a well healed pedicle graft had been put on the stump of the thumb. He could not abduct or oppose the stump of the right thumb, flexion of the right middle finger being prevented. There was shocklike tenderness over the medial and lateral aspects of the stump (Fig. 7*A*).

palmar aponeurosis were excised. Two neuromas were removed from the right thumb. Two crossed Kirchner wires maintained a satisfactory relation between the 1st metacarpal, the proximal phalanx and the stump of the 2d metacarpal bone (Fig. 7*B*). The abdominal-tube skin graft was used to cover the skin defect in the web. Satisfactory opposition of the thumb stump resulted, and there was good pinch ability between the thumb and tips of the right middle, ring and little fingers (Fig. 7*C*).

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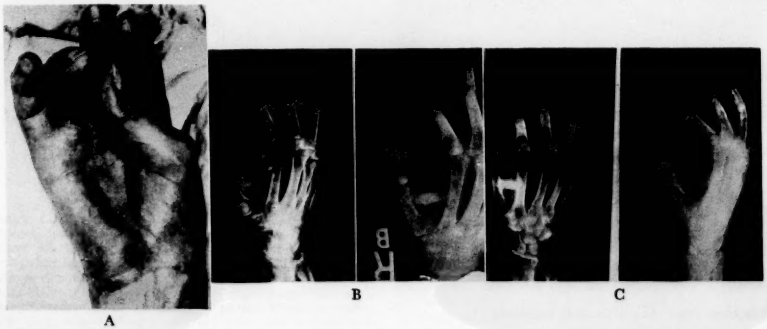
FIGURE 9. *Subluxation of the Carpometacarpal Joint of the Thumb Causing Adduction Contracture in Case 9* (A), *with Satisfactory Opposition after Operation* (B).



A B C

FIGURE 10. *Adduction Contracture after Excessive Exposure in a Steam Bath in Case 10* (A), *Showing Bone Graft Not Completely Healed Six Months* (B) *and Completely Healed Twelve Months after Operation* (C).

An abdominal-tube skin graft was constructed. In the correction of the adductor contracture the adductor pollicis muscle, the 1st dorsal interosseous muscle and a part of the

CASE 8. A 27-year-old soldier was shot in combat in Korea by a machine-gun bullet in the left hand. The wound of entry was on the dorsum of the left thumb, and the wound of exit on the palm of the hand. Five operations had been performed: an initial débridement and cleansing; an intermediate-thickness skin graft of the palm; an abdominal-pedicle skin graft on the palm; excision of slough and a pedicle skin graft; and an opponens-tendon transfer using the sublimis tendon of the ring finger.

Adduction Contracture after Dislocation of the Thumb

CASE 9. A 36-year-old man fell a distance of 5 feet from a ladder in his shop. There was a dislocation of the greater multiangular 1st metacarpal joint and a fracture of the proximal thumb phalanx, with consequent adduction contracture of the right thumb (Fig. 9*A*).

At operation, an arthrodesis of the right greater multiangular 1st metacarpal joint was performed, fixation being

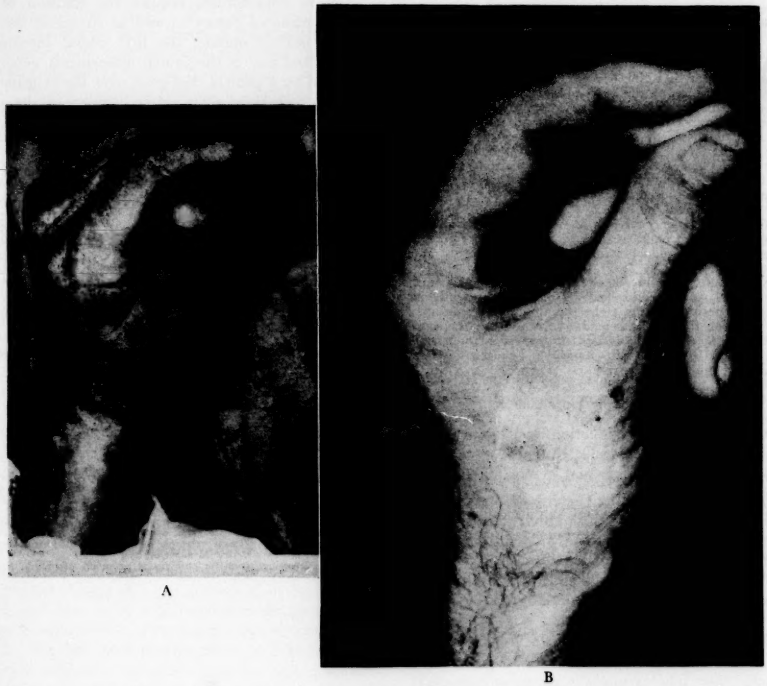


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FIGURE 11. *Adduction Contracture Caused by Injury of the Brachial Plexus at Birth in Case 11* (A), *with Opposition Restored after Tendon Transfer* (B).

When the patient was first examined at the Veterans Administration Hospital, Boston, 3 years after injury, he could not oppose or abduct the left thumb. The index finger brushed the thumb on flexion. There was shocklike tenderness in the scar over the lateral aspect of the tip of the little finger. A pedicle skin graft over the thenar area was healed (Fig. 8*A*).

In reconstruction of the thumb, the adductor pollicis muscle, the 1st dorsal interosseous and a part of the palmar fascia were excised. Satisfactory relation between the 1st and 2d metacarpals was maintained by 2 crossed Kirchner wires. A neuroma was excised from the little finger. The previously applied pedicle skin graft provided adequate coverage for the skin defects. The Kirchner wires were removed in 9 weeks. Good opposition and good pinching power between the thumb and the tips of the index, middle and ring fingers resulted (Fig. 8*B*).

provided by 2 Kirchner wires. Good abduction and opposition, as well as good pinch power and grasp between the thumb and other fingers, resulted (Fig. 9*B*).

Deep Burn Causing Adduction Contracture

CASE 10. A 50-year-old man fell asleep in a steam bath and received a 2d-degree burn of the right hand. Adduction contracture of the right thumb gradually developed. On physical examination 2 years later, there was a severe adduction contracture of the right thumb, the result of poor splinting. He was unable to abduct and oppose the thumb, and flexion of the index and middle fingers was obstructed (Fig. 10*A*). X-ray examination revealed a severe displacement of the distal end of the 1st metacarpal bone on the 1st phalanx of the right thumb.

At operation an incision was made through the thumb-

index web. The insertion of the adductor pollicis was incised, and the 1st dorsal interosseous and part of the palmar fascia were excised. Proper position of the 1st metacarpal in relation to the proximal phalanx was maintained with difficulty, and it was deemed necessary to use a bone graft to preserve the new position. A piece of rib from a bone bank was inserted into the cleft between the 1st and 2d metacarpals. The skin coverage was adequate. The bone graft was solidly healed in 12 months (Fig. 10*B* and *C*). Good opposition resulted.

Adduction Contracture of the Thumb Resulting from Paralysis at Birth

CASE 11. A 28-year-old man had suffered an injury to the left brachial plexus at birth. Four months after birth, a partial paralysis of the left arm was noted. At 2 years of age, an operation on the left brachial plexus was performed at the Children's Hospital in Boston. At the age of 15 years, a diagnosis of spastic monoplegia of the left arm, because of the birth injury, was made at the Peter Bent Brigham Hospital, where the activity of the flexor muscles was said to have been much greater and stronger than that of the extensor muscles of the paralyzed arm. A tendon transfer of the flexor carpi ulnaris to the extensor carpi radialis had been performed.

When the patient was first seen at the Boston City Hospital, at the age of 28 years, the outstanding disorder was a severe spastic adduction contracture of the right thumb (Fig. 11*A*).

At operation, the insertion of the adductor pollicis muscle was incised, and a tendon transfer operation was performed to aid opposition of the right thumb. To accomplish this the slips of the sublimis tendon of the ring finger were inserted into the head of the 1st metacarpal and base of the proximal phalanx. Fair opposition between the thumb, index and middle fingers resulted (Fig. 11*B*).

Summary and Conclusions

A hand with an adduction contracture of the thumb is greatly disabled. It is unable to exercise its main functions of pinch and grasp, and is usually only a useful hook.

The commonest causes of adduction contracture of the thumb are trauma and burns. Illustrative cases caused by burns and trauma to the skin, crushing injuries to deep tissues, an avulsed wound and ischemia, war wounds, a dislocated thumb, deep thermal burn and paralysis of the brachial plexus at birth are presented.

Adduction contracture of the thumb can usually be prevented by proper splinting.

Deforming skin contractures can often be corrected by excision of any scar and skin grafting or by Z-plasty.

Deeper contractures require the excision of all deep contracted tissues as well as (usually) the adductor pollicis muscle, the first dorsal interosseus muscle, and part of the palmar aponeurosis, generally followed by a pedicle skin graft over the skin defect. On rare occasions when, after excision of the scar, opposition or apposition is difficult to maintain, especially as part of birth paralysis, or when recurrent contractures occur, a bone strut may be used. Usually, however, crossed Kirchner wires are adequate to maintain the proper relations between the first and second metacarpals and the proximal phalanx. The wires are removed in an average of nine weeks. In most cases, some active rotation of the thumb or its remnant results. Tendon transfer to help re-establish active opposition may be necessary in some cases.

I am indebted to Dr. Donald Munro for his constructive criticisms and suggestions.

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A STUDY OF ILLNESS IN A GROUP OF CLEVELAND FAMILIES*

IX. Recognition of Family Epidemics of Poliomyelitis and Pleurodynia during a Search for Respiratory-Disease Viruses

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THE continuing development and improvement of tissue-culture methods have simplified the study of infectious agents, such as poliomyelitis[1,2] and Coxsackie[3] viruses, originally isolated in animal hosts, and have made possible the primary isolation of previously unidentified viruses.[4-7] Of the last group, some, often referred to as "orphan" viruses, have not yet been related clearly to disease[6,7]; others, variously designated as the adenoidal-degeneration (AD), respiratory-infection (RI), acute-respiratory-disease (ARD) or adenoidal-pharyngeal-conjunctival (APC) group of viruses,[4,5,8-11] have been related etiologically to certain respiratory diseases.[8-13]

Interest in this new group of respiratory viruses prompted a study of their role in the causation of the many respiratory infections occurring in a group of families under constant observation.[14] Nonbacterial pharyngitis caused by the adenoidal-degeneration Type 3 virus had occurred in this population during the summer of 1954,[13] but antibody studies indicated that infection with the virus of acute respiratory disease (Hilleman's RI-67 or Huebner's adenoidal-pharyngeal-conjunctival virus Type 4) had not occurred for some time.[15] Yet the marked increase in the incidence of respiratory disease noted each year with the opening of school[14] resembled somewhat the behavior of acute respiratory disease in military recruits.[16] Accordingly, specimens were collected from all persons during this crucial period in September, 1954, and from those with respiratory symptoms during selected intervals in subsequent months until May, 1955. The frequency of occurrence of infection with the new respiratory viruses during this winter season has been measured also by serologic tests, and the results of the isolation and antibody studies will be presented elsewhere. It is the purpose of this report to describe the type of "by-product" information pertaining to other viruses that was obtained during this study, and to emphasize the importance of the family unit in the spread of disease. Because of the range of sensitivity of the cells now being widely used in tissue culture, particularly HeLa cells,[17] it is expected that others undertaking the investigation of family groups will have similar experiences.

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Conducted under the sponsorship of the Commission on Acute Respiratory Diseases, Armed Forces Epidemiological Board, and supported in part by the Office of the Surgeon General, Department of the Army, and by grants from the Brush Foundation, the Robert Hamilton Bishop, Jr., Endowment Fund, Mr. Philip R. Mather and the Republic Steel Corporation.

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MATERIALS AND METHODS

The general methods used in the study of the families[14] and in the propagation of HeLa-cell cultures[11] have been described elsewhere. Specific modifications in tissue-culture methods were as follows: the nutritive medium employed was composed of 40 per cent human serum and 60 per cent Hanks balanced salt solution; the maintenance fluid was composed of 10 per cent chicken serum, 15 per cent tryptose phosphate broth[18] and 75 per cent synthetic maintenance solution.[2] Penicillin and streptomycin were added to make a final concentration of 100 units and 0.1 mg. per ml. of each, respectively.

Specimens

At the time of collection pharyngeal swabs were placed in 2 ml. of either Hanks balanced salt solution or tryptose phosphate broth, and were transported to the laboratory within thirty to a hundred and eighty minutes. The tubes were then sealed and stored at −70°C. Between September 27 and November 30, 1954, 474 specimens were collected, and 196 were examined.

Isolation Attempts

HeLa-cell tubes were washed twice with Hanks balanced salt solution, and infecting fluid added. Initially, 0.1 ml. of specimen was added to 0.9 ml. of maintenance fluid in each of 8 tubes; subsequently, 0.2 ml. of specimen was added to 0.8 ml. of infecting fluid in each of 4 tubes. The cells were observed daily for the development of degenerative changes. As the maintenance fluid became acid, it was replaced, such replacement being necessary two or three times during the twelve to fourteen days of observation. When specific cytopathogenic changes occurred, cells still adherent to the glass were removed with a rubber policeman and disintegrated in the infecting fluid by freezing and thawing six times. The supernatant fluid was stored in sealed glass ampoules at −70°C. until passed to another set of tubes or to a bottle of HeLa cells. In some cases, particularly near the end of the

two weeks of observation, in which the specific nature of any degeneration was in doubt, the tubes were harvested and passed.

Neutralization tests were performed as described previously,[11] with minor modifications. An estimated 100 ID_{50} of virus was used. The poliomyelitis viruses isolated were identified and typed by neutralization with specific antiserums.* Of the Coxsackie viruses, were used. Three tissue-culture tubes of HeLa cells per dilution were employed for the poliomyelitis titrations, and 2 tubes per dilution for the Coxsackie titrations. Titers were expressed as reciprocals of the final dilutions of serum in the serum-virus mixture that protected half the tubes from the cytopathogenic effects of poliomyelitis virus or protected all tubes from Coxsackie virus. The poliomyelitis viruses isolated were all Type 1; therefore, the presence or absence of antibody to Types 2 and 3 was assayed only at a final serum dilution of 1:5.

TABLE 1. *Type 1 Poliomyelitis Virus in Family 29.*

Subject No.	Age	Date of Onset	Symptoms	Virus Isolation	Titer of Antibody in Serum			
					Date	Type 1	Type 2	Type 3
	yr.							
2	36	9/29/54	Irritated throat	10/1/54	4/ 1/53	<5	>5	<5
					4/15/54	<5	nt†	nt†
					10/24/54	>5	>5	5
				+	12/22/54	>320	>5	<5
4	10	10/ 2/54	Constitutional* Temp. 101°F. Abdominal pain	10/1/54	4/ 1/53	<5	>5	<5
					4/15/54	<5	nt†	nt†
					10/24/54	>5	>5	<5
				+	12/29/54	200	>5	<5
1	36		None	10/1/54	5/10/53	<5	<5	<5
					4/11/54	<5	nt†	nt†
					10/24/54	>5	<5	<5
				—	1/6/55	128	<5	<5
3	13		None	10/1/54	4/ 1/53	<5	>5	<5
					4/15/54	<5	nt†	nt†
					10/24/54	>5	>5	>5
				+	12/29/54	>320	>5	5
5	4		None	10/1/54	4/ 1/53	<5	>5	<5
					4/15/54	<5	>5	<5
					10/24/54	>16	nt†	nt†
				—	12/29/54	>320	>5	<5

*Fever and malaise.
†Not tested.

TABLE 2. *Type 1 Poliomyelitis Virus in Family 83.*

Subject No.	Age	Date of Onset	Symptoms	Virus Isolation	Titer of Antibody in Serum			
					Date	Type 1	Type 2	Type 3
	yr.							
5	3	10/ 6/54	Nasal obstruction & cough	No specimen	3/19/52	<5	<5	<5
					2/26/55	>320	<5	<5
4	5	10/18/54	Anorexia, nasal obstruction, sore throat, vomiting & temperature of 104°F.	10/19/54	No serum			
				+				
3	7	10/19/54	Nasal obstruction, irritated throat & temperature of 102°F.	10/19/54	4/21/53	<5	<5	<5
					9/ 2/54	<5	nt*	nt*
				+	2/26/55	200	<5	<5
2	32	—	None	No specimen	4/21/53	<5	<5	<5
					9/30/54	<5	nt*	nt*
					2/26/55	16	<5	<5
1	33	—	None	No specimen	4/26/53	<5	>5	<5
					9/11/54	<5	nt*	nt*
					3/16/55	<5	>5	<5

*Not tested.

one strain from Family 37 (see Table 5) was identified by Miss Grace M. Sickles[3] in Dr. Gilbert Dalldorf's laboratory as Coxsackie, Group B, Type 3. The other strains isolated from this family were similarly typed by means of specific antiserums kindly supplied by Miss Sickles. For serum neutralization titrations, standard laboratory strains of poliomyelitis viruses* and the Coxsackie virus isolated from subject 37-4

*Kindly supplied by Dr. Jonas Salk.

Serums

Serum specimens are collected routinely from all subjects in the spring and fall. The fall specimens, 1954, were employed as "acute-phase" serums. Convalescent-phase specimens were collected after isola-

tion of the viruses. All serums were stored at −20°C. and were heated at 56°C. for thirty minutes before use.

Results

Through the collection of pharyngeal swabs from persons with respiratory symptoms in October and the family were examined. Virus was isolated from the thirteen-year-old daughter who had reported no symptoms. Neutralization tests indicated that Type 1 antibody had appeared in routine serum specimens obtained three weeks after the collection of the throat swabs. Titration of subsequent serums demonstrated that significant increases in titer of Type 1 antibodies developed in all 5 members of the family.

Table 3. *Type 1 Poliomyelitis Virus in Family 80.*

Subject No.	Age	Date of Onset	Symptoms	Virus Isolation	Titer of Antibody in Serum			
					Date	Type 1	Type 2	Type 3
	yr.							
4	3	10/28/54	Anorexia; vomiting (twice); temperature of 102°F.; patient febrile for 3 days.	No specimen				
		11/ 5/54	Coryza; mild pharyngeal injection.	11/5/54	4/15/53	<5	<5	<5
				+	1/25/55	160	<5	<5
					5/10/53	<5	>5	<5
1	35	11/ 3/54	Irritated throat	No	9/11/54	<5	Nt*	Nt*
				specimen	1/25/55	<5	>5	<5
3	6	11/ 8/54	Coryza	11/8/54	4/15/53	<5	<5	<5
				—	5/26/55	>320	>5	<5
					4/15/53	>5	>5	<5
2	33	(Patient not ill)	None	No	9/11/54	<5	Nt*	Nt*
				specimen	1/25/55	9	>5	<5

*Not tested.

November, the occurrence of Type 1 poliomyelitis infections in 3 families and of Group B Coxsackie virus infections in 1 family was discovered. These family

Type 1 poliomyelitis viruses were isolated from 2 children in Family 83 (Table 2) from specimens collected in mid-October. At this time, only persons with

Table 4. *Tests for Virulence in Cynomolgus Monkeys of Type 1 Poliomyelitis (Viruses) Isolated from Members of Families 29 and 80.**

Strain	Route	TCD_{50} Inoculated	Monkey No.	Paralysis	Poliomyelitis Lesions
"29-2"	Intracerebral	$10^{4.1}$	7665	Partial, lower extremities, on 7th day	+
			7666	None	+
HeLa passage 2			7667	Partial, lower extremities, on 15th day	+
Cynomolgus kidney passage 1		$10^{7.1}$	7668	Left hemiplegia on 4th day	+
			7669	Death on 2d day	
$10^{7.4}TCD_{50}$/ml.			7670	?	+
"80-4"	Intracerebral	$10^{4.2}$	7671	None	+ focal
			7672	None	0
HeLa passage 3			7673	None	+
Cynomolgus kidney passage 1		$10^{7.2}$	7674	None	+ focal; slight.
			7675	None	+ focal; very slight.
$10^{7.9}TCD_{50}$/ml.			7676	None	+ focal; medulla only.
"80-4"	Intracerebral	$10^{6.2}$	7866	None	+
			7867	None	+
Cynomolgus kidney passage 5			7868	None	+
			7869	None	+
Progeny of 3 terminal dilution purifications	Spinal	$10^{5.5}$	7870	Lower extremities only on 5th day	+
			7871	Progressive on 3d day	+
$10^{7.5}TCD_{50}$/ml.			7872	None	0 - ?
			7873	None	+

*Performed by Dr. Albert B. Sabin.

epidemics are summarized in Tables 2, 3 and 5.

Pharyngeal swabs were collected from all members of Family 29 (Table 1) on October 1. Those from subjects 2 and 4 were processed because they had respiratory symptoms within three days of the routine collection of the specimens. When poliomyelitis virus was isolated from the mother and the ten-year-old son, specimens from the other 3 members of selected respiratory illnesses were being cultured. No serums were available from 1 of these children; the other child and a younger sibling showed significant increases in titer of Type 1 antibodies. The mother had a very slight increase in titer; the father gave no serologic evidence of infection. The grippelike illnesses in subjects 3 and 4 were consistent with severe common colds or acute respiratory disease. It is of

some interest that these 2 girls were scheduled for tonsillectomy, the operation being cancelled because of the development of the symptoms noted.

In November an effort was made to collect pharyngeal swabs in broth from all persons with respiratory symptoms. It is unfortunate that one was not obtained from the father (Subject 1) of Family 80 or the mother (Subject 2) of Family 37. Type 1 poliomyelitis virus was isolated from 1 of the 2 children in Family 80 (Table 3). Serologic evidence of infection with Type 1 virus developed in both; the mother, with no significant change in titer, and the father escaped infection.

The virulence of two of these strains was tested by Dr. Albert B. Sabin[19] in cynomolgus monkeys (Table 4). Strain "29-2" caused partial paralysis in some of the monkeys given large amounts of virus by the intracerebral route. Strain "80-4" produced histologic lesions but no paralysis after intracerebral inoculation in 10 monkeys; on intraspinal inoculation of $10^{5.5}$ TCD_{50} this strain resulted in paralysis in 2 of 4 monkeys.

Study of the illnesses in Family 37 (Table 5) afforded an excellent illustration of the spread of Coxsackie virus infections among the members of a household. During a ten-day period, 7 of the 8 members of the family became ill, only the three-month-old infant having no recognized illness. The clinical manifestations were strikingly similar as the disease progressed through the family, the illness being characterized by fever, headache and such respiratory symptoms as coryza, sore throat or cough and chest pain. The adults were better able to describe this pain as a generalized aching throughout the muscles of the thorax. Viruses isolated from 3 of the children were identified as Coxsackie, Group B, Type 3. All the 6 subjects tested showed significant increases in titer of antibodies for this virus.

Discussion

In the absence of the studies described, it is likely that the illnesses observed in Families 29, 80, and 83 would have been classified as belonging to the heterogenous group of common respiratory diseases. Indeed, it is possible that the symptoms recorded were due to unidentified respiratory viruses, and were not produced by or etiologically related to the poliomyelitis viruses shown to be present in the throats. Virus is present in the throat during the acute stage of poliomyelitis,[20] but inapparent infections have usually been recognized by stool surveys. Several investigators,[21-23] by examination of stools, respiratory secretions and blood, have documented the importance of the family unit in the spread of poliomyelitis. Of particular interest here is the fact that poliomyelitis viruses were present in the throats of the members of these families in the fall at a time when paralytic disease had disappeared from the community and, further, that none of the concomitant illnesses resembled clinical poliomyelitis. Although the symptoms that did occur cannot necessarily be attributed to the virus, sufficient viral antigen was produced to stimulate antibody production.

Since the poliomyelitis viruses had not caused either paralysis or recognizable nonparalytic disease, they were submitted to Dr. Albert B. Sabin because of his interest in finding avirulent strains. Dr. Sabin[19] reported as follows:

> Unpublished studies on a large number of strains of poliomyelitis viruses indicate the existence of a wide spectrum of pathogenicity for primate neurons. At the most severe end of the spectrum are strains that readily multiply in and damage chimpanzee as well as monkey neurons. In the middle of the spectrum are viruses that, though still paralytogenic for monkeys by intracerebral as well as by spinal inoculation, are not paralytogenic for chimpanzees even after direct spinal inoculation of 10^6 TCD_{50} or more. At the most attenuated end of the spectrum

Table 5. *Coxsackie Virus, Group B, Type 3, in Family 37.*

Subject No.	Age	Date of Onset	Symptoms	Date of Specimen	Virus	Titer of Antibody in Serum	
						Date	Titer
	yr.						
4	10	10/31/54	Headache, malaise, coryza, cough, chest pain & temperature of 101°F.	11/2/54 11/5/54	+ +	10/10/54 12/17/54	<4 256
1	38	11/3/54	Headache, coryza, irritated throat, cough, & aches in back and chest; patient feverish.	11/5/54	—	10/10/54 12/31/54	<4 16
6	6	11/3/54	Headache, malaise, sore throat and chest pain; patient feverish.	11/5/54	—	10/10/54 12/17/54	<4 64
5	9	11/6/54	Headache, malaise, sore throat, chest pain & temperature of 103°F.	11/9/54	+	10/10/54 12/17/54	<4 256
7	1	11/7/54	Malaise, listlessness & temperature of 102°F.	11/9/54	+	(No serum)	
3	13	11/9/54	Headache, malaise, sore throat, chest pain & temperature of 101°F.	11/9/54	—	10/10/54 12/16/54	<4 256
2	37	11/10/54	Headache, malaise, coryza, sore throat & pains in chest, shoulders and trunk; patient feverish.	None		10/10/54 12/16/54	<4 256
8	1/4	Not ill	None	None		(No serum)	

are strains that not only are avirulent by intracerebral inoculation in monkeys but also require the direct spinal inoculation of more than 10^5 TCD_{50} to produce a localized nonprogressive paralysis in an occasional monkey . . . The small proportion of paralytic infections in human beings suggests that human neurons are either even more resistant than those of chimpanzees or at worst of a similar order of resistance. The quantitative tests . . . performed in monkeys with the poliomyelitis strains recovered from families 29 and 80 [Table 4] indicate that they belong at the attenuated end of the spectrum that would be expected to be nonparalytogenic for chimpanzees in the maximum dosage.

Coxsackie viruses were isolated from only one family, and although infection spread throughout this family, no similar illnesses were observed in other members of the population. Whereas this was a striking family epidemic, and the illness was similar in all cases, the disease was not recognized clinically as pleurodynia until the causative agent was identified. Like poliomyelitis viruses, Coxsackie viruses are found, and commonly sought for, in feces. However, the Group A viruses produce an infection of the respiratory tract, herpangina,[24] and Group B viruses have been previously recovered from respiratory secretions.[25] The Group B, Type 3, virus was one of the first related to pleurodynia.[26]

Just as extensive examination of stool specimens in tissue cultures has led to the discovery of new viruses, many of them still "orphans," so similar study of respiratory tissues and secretions has permitted the identification of a new group of agents, some still not definitely related to disease. It is apparent, also, that the search for "new" agents will continue to contribute information about "old" viruses.

Summary

A study primarily designed to measure the importance of the recently identified respiratory viruses — acute-respiratory-disease, respiratory-infection or adenoidal-pharyngeal-conjunctival group — as the cause of respiratory illnesses in a population of families also resulted in the identification of poliomyelitis and Coxsackie infections. Material from pharyngeal swabs collected in October and November, when inoculated into HeLa-cell cultures, yielded Type 1 poliomyelitis viruses from 6 members of 3 families, and Coxsackie, Group B, Type 3, viruses from 3 members of 1 family. These subjects and some of the other members of their families showed increases in titer of antibodies for the respective viruses.

We are indebted to Mrs. Mary G. Stokes, Miss Dorothy Sanderson, Miss Juanita J. McConnell and Mr. Ernest I. Stewart for their assistance during this study.

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FREQUENCY OF THE ASYMPTOMATIC LOWER ESOPHAGEAL CONTRACTILE RING*

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WITHIN recent years several papers have identified a ringlike narrowing or constriction in the terminal portion of the esophagus as a cause of dysphagia[1-3] (Fig. 1). Although this narrowing had been observed before these reports and described as an annular indentation in the phrenic ampulla, little clinical significance was attached to its presence.[4] That the constriction is capable of producing symptoms was demonstrated by the feeding of a barium-

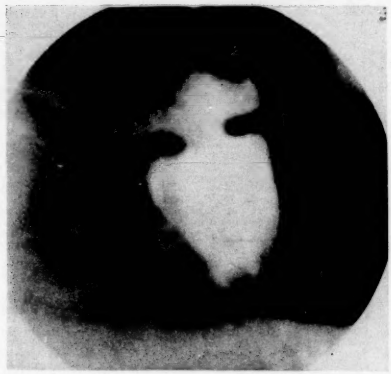

FIGURE 1. *Spot Film of the Lower Esophagus, Demonstrating a Symptomatic Contractile Ring.*

This sixty-nine-year-old man had suffered from intermittent dysphagia for four years. After a bread-barium swallow (not shown here), he complained of dysphagia, and the bread could not be seen obstructing the residual esophageal lumen.

bread or barium-steak meal or barium-filled gelatin capsules to patients who did not have any obvious cause for their dysphagia but did have an annular constriction on x-ray study. After these substances had been ingested they complained of dysphagia; on fluoroscopy the barium food or barium capsules could be seen impacted in the esophagus at the level of the ring and obstructing the residual esophageal lumen.

Patients with rings that cause symptoms present a fairly typical clinical picture; they complain of intermittent dysphagia, often of years' duration. Lower substernal distress is frequently associated with the dysphagia; the patient states that he feels a moderate or severe "sticking" pain in a sharply localized area over the lower end of the sternum. The distress and sensation of esophageal occlusion last from minutes to hours; the patient may then feel the bolus "working through." A residual lower substernal discomfort sometimes persists for several hours. During moderate attacks the patient drinks water to "wash the food down," but during severe attacks he abstains from all liquids or foods because he is afraid to swallow anything.

Attacks may vary in frequency: in severe cases symptoms appear with ingestion of any solid food; in milder cases only certain foods such as bread or meat (particularly roast beef or steak) will precipitate dysphagia and pain. If food is bolted rapidly, symptoms are more apt to occur. By avoiding certain foods or by careful mastication, patients may prevent attacks for weeks or months.

The diagnosis of this unusual condition depends on the radiographic demonstration of the ring since it has not been observed by esophagoscopy in the cases that I have seen. On x-ray study the narrowing appears as a sharply demarcated negative shadow, ringlike in character, 2 to 6 mm. in breadth, intersecting the esophagus at right angles to the long axis, and 2 to 6 cm. above the cardioesophageal junction. As yet the nature of this ringlike narrowing has not been defined; it has been described as a herniated esophagogastric junction by one group[5] and as a contractile ring by another.[1]

Rings have been observed in patients without dysphagia, the frequency being given as 1 or 2 per cent.[5] Specific data on the method of deriving these figures are lacking. Information concerning the existence of asymptomatic rings is of more than theoretic importance. If this structure is found often in routine radiographic studies of the esophagus, it may be an incidental finding in patients with esophageal symptoms. Realization that it is not uncommon would prevent errors in diagnosis — for example, dysphagia combined with a ring on the x-ray film may not necessarily mean a cause-and-effect relation. A situation similar to that which frequently arises in the problem of hiatus hernia would thus be avoided; too often the hiatus hernia is blamed for a patient's complaints because it may be the only positive radiographic finding in patients with vague upper gastrointestinal symptoms. To determine the frequency of asymptomatic rings, fluoroscopy was carried out in 100 patients without esophageal symptoms.

METHOD OF STUDY

Each of the 100 patients was examined after a barium swallow without any special technic except

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that routinely followed in performing esophagograms. The barium-water mixture was of the consistence usually employed in routine gastrointestinal radiography with the tap water approximating room temperature. Early in the study the examination was performed with the patient in the horizontal right anterior oblique position, but the last 25 patients were examined in this position as well as in the horizontal left posterior oblique position. Admittedly, the patients studied were a select group since many were undergoing routine fluoroscopy for digestive complaints although a number examined did not have gastrointestinal symptoms or disease. However, no patient was included in this series if he had dysphagia or symptoms suggestive of esophageal disease. The youngest subject was fourteen and the oldest eighty-four years of age. Fifty-two patients did not have objective evidence of organic gastrointestinal disease (18 had no disease and 34 had functional gastrointestinal disease); 37 patients had had or were having active peptic ulcers, 24 of which were duodenal.

TABLE 1. *Summary of Data in Patients with Asymptomatic Esophageal Contractile Ring.*

PATIENT	AGE	SEX	DIAGNOSIS	RADIOGRAPHIC CHARACTERISTICS	
				BREADTH OF RING	WIDTH OF RESIDUAL ESOPHAGEAL LUMEN
	yr.			*mm.*	*mm.*
L.C.	72	M	Healed duodenal ulcer	6	10
H.F.	56	M	Functional gastrointestinal disease	7	11
L.S.	35	M	Functional gastrointestinal disease	6	7
L.A.	57	M	Healed duodenal ulcer	3	23
J.H.	25	M	Active duodenal ulcer	3	25
W.E.	63	F	Healed duodenal ulcer	4	25

RESULTS

In the 100 patients examined radiographically a definite narrowing characteristic of a contractile or constriction ring was seen in 6 patients. Descriptive data concerning these 6 patients are given in Table 1. Indentations suggestive of a ring were noted in one patient (Fig. 2*C*), but this case was not included as an example of an esophageal ring. Position of examination was important in detecting the ring in 1 patient: it was not seen in the right anterior oblique position but was easily observed in the left posterior oblique.

The asymptomatic rings varied from 3 to 7 mm. in breadth. Three of the subjects demonstrated rings of such magnitude that the residual esophageal lumen was reduced to 7 to 11 mm. The rings in these subjects did not differ from those previously described in some patients with severe dysphagia. In the other 3 subjects only minor reduction in the esophageal lumen occurred, the residual barium column being 23 to 25 mm. in diameter.

Five of the 6 subjects were males twenty-five to seventy-two years of age, and the sixth was a woman of sixty-three. Four had had or were having symptoms of duodenal ulcer confirmed by x-ray examination of the duodenum; the remaining 2 suffered from

A B C

FIGURE 2. *Roentgenograms in 3 Patients with Esophageal Rings.*

A = *film in L.C., a seventy-two-year-old man, demonstrating an asymptomatic lower esophageal contractile ring similar to that seen in patients with severe dysphagia.*

In W.E., a sixty-three-year-old woman, the ring is only moderately developed, and the encroachment on the esophageal lumen is slight (B).

Film of G.H., a thirty-six-year-old woman, shows indentations in the lower esophagus suggestive of a contractile ring (C); *a true ring was never observed during the fluoroscopic examination.*

functional gastrointestinal disorders. In the 94 patients without rings the diagnosis of duodenal ulcer was made in 20 patients, a rate of 21.3 per cent. The association of duodenal ulcer and these rings was also observed in patients with symptomatic contractile rings.

Discussion

The data presented suggest that the frequency of asymptomatic rings, 6 per cent, is higher than that previously reported, 1 or 2 per cent. The true figure for the general population would be difficult to deduce from these data since the subjects studied were a selected group, only 18 of whom did not have gastrointestinal symptoms. The group on the whole was probably similar to that observed by Gary and Schatzki,[5] whose patients presumably were also undergoing radiographic study for gastrointestinal complaints.

It has been postulated that the lower esophageal ring[1] corresponds to the inferior esophageal sphincter of Lerche.[6] The finding that asymptomatic rings are relatively frequent would be consistent with this assumption; these constrictions appear to be an exaggerated manifestation of a normal structure. Other evidence that the contractile ring and the inferior esophageal sphincter are the same was that obtained by Respess,[7] who, by a special technic of chilling the esophagus, was able to demonstrate a ringlike constriction in 7 of 31 patients who did not show a ring on routine fluoroscopy. The ring produced in some of his subjects by this method was similar to that observed in patient W. E. (Fig. 2*B*). Still unanswered is the question why the ring is symptomatic in some persons and not in others although this structure is similar in appearance in both groups.

Aside from the theoretic aspects, a consideration of practical importance arises with the finding of 6 per cent asymptomatic rings. Just because the ring exists does not necessarily mean that it is the cause of a patient's dysphagia. Before the narrowing is accepted as the cause of symptoms, the patient should be subjected to a food-barium or barium-capsule test. If the dysphagia is thereby reproduced and the barium material at that time is seen impacted in the esophagus at the site of the constriction, the ring can be accepted as the cause of dysphagia.

Summary and Conclusions

Six of 100 patients without esophageal symptoms and undergoing routine fluoroscopy after a barium swallow were shown to have lower esophageal rings. In 3 of the 6 the ring was similar in size and appearance to that of patients suffering from severe dysphagia. It is suggested that before such a ring is accepted as the cause of dysphagia the patient should be subjected to a barium-food or barium-capsule test.

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SPONTANEOUS PNEUMOPERITONEUM IN THE NEWBORN

Report of a Case

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IN 1954 a two-day-old infant was admitted to the Rhode Island Hospital with pneumoperitoneum. At operation no abnormality could be found to explain the free air in the peritoneal cavity. The baby recovered without complications. A review of the current literature revealed only 2 similar cases, reported by Birdsong and Frame[1] in 1951. The rarity of this abnormality prompted the following additional report.

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Case Report

B. B., a 2-day-old male infant, was referred to the private surgical service of the Rhode Island Hospital because an x-ray film had shown free air in the peritoneal cavity. He had been delivered at full term (by cesarean section) on March 30, 1954, at the Providence Lying-In Hospital. The mother was a 29-year-old woman who had a double uterus and vagina. The baby's birth weight was 2.9 kg. (6 pounds, 9 ounces). There were no complications during delivery. After birth normal breathing began without artificial stimulation or aspiration. Several hours after birth the baby took his 1st feeding without vomiting. Shortly thereafter he passed a normal meconium stool. On the 2d day his respirations became somewhat labored and rapid. At this time

mild circumoral and extremity cyanosis were observed. X-ray examination of the chest showed free air in the peritoneal cavity, and he was transferred to the Rhode Island Hospital at 20 hours of age for definitive therapy.

Physical examination showed a well developed, well nourished baby with obviously increased, slightly labored respirations. There was minimal cyanosis of all extremities. The abdomen was soft, distended, tympanitic and diffusely tender; on auscultation there was no audible peristalsis. The patient had a meconium stool and voided clear urine after digital examination of the rectum, which was normal.

The temperature was 99.6°F., the pulse 140, and the respirations 45.

Review of the films of the chest and abdomen in the upright position, taken at the Providence Lying-In Hospital before transfer, showed a large amount of free gas in the peritoneal cavity below both leaves of the diaphragm (Fig. 1). The gas pattern in the bowel was interpreted as normal, without evidence of obstruction. The heart and lungs were normal. The etiology of the free air was undetermined, but because of the likelihood of a perforation of the gastrointestinal tract, surgical exploration was undertaken without further investigation. Under open-drop ether anesthesia the abdomen was entered through a long right-rectus-lateral-muscle-retracting incision. When the peritoneum was opened there was an escape of air and a small amount of clear, dark-colored, free fluid. A culture was taken (this was later reported as sterile). The gastrointestinal tract was then carefully examined from the esophagogastric junction to the rectum at the level of the pelvic floor. No signs of any abnormality or perforation were found. There was no evidence of a previous intra-uterine meconium peritonitis. The peritoneal cavity was filled with warm, physiologic saline solution, and no bubbles of air escaped through the fluid medium. This solution was removed by suction, and the abdomen was closed without drainage.

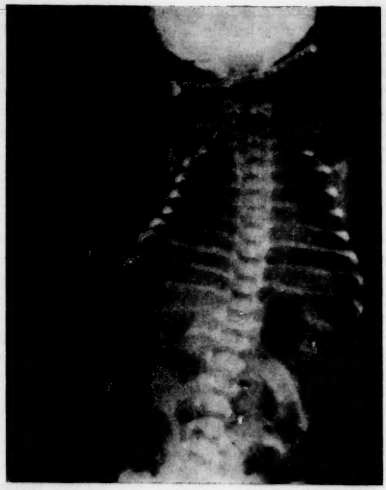

FIGURE 1. *Roentgenogram Taken at Twenty Hours of Age, Demonstrating Free Gas in the Peritoneum, without Evidence of Intestinal Obstruction.*

Postoperatively, the patient was placed on nasal gastric suction, penicillin and intravenous infusions of fluids. The abdomen remained soft. The gastric suction was discontinued on the 2d postoperative day after he passed gas and meconium by rectum. At this time auscultation of the abdomen showed return of normal peristalsis. Several oral feedings of dextrose and water having been retained on the 2d postoperative day, an evaporated-milk formula was started. These feedings were well tolerated, and he had normal milk stools. A film of the abdomen on the 4th postoperative day showed no free intraperitoneal air (Fig. 2). He gained weight and was discharged home on the 12th day. Follow-up studies at regular intervals showed an uneventful course.

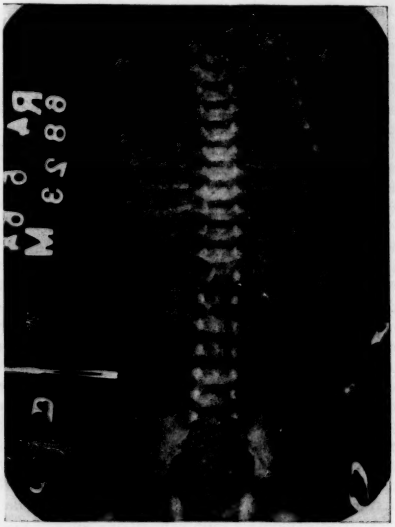

FIGURE 2. *Roentgenogram Taken on the Fourth Postoperative Day, Demonstrating a Normal Gas Pattern in the Abdomen.*

PATHOLOGY

Pneumoperitoneum in the newborn, accompanied by intestinal obstruction and perforation of the gastrointestinal tract above the point of obstruction, is well understood. This form of pneumoperitoneum is associated with such abnormalities as atresia or stenosis of the intestinal tract, meconium ileus, mid-gut volvulus and strangulated hernia. Other pathologic conditions complicated by perforation and free air in the peritoneal cavity in the newborn include mesenteric thrombosis, perforated peptic or bacterial ulcerations, ruptured diverticula, and perforations secondary to trauma. Potter[2] mentions a fatal case in an infant who appeared normal for the first twenty-four hours and then became acutely ill. Air was noticed in the peritoneal cavity on x-ray study. At autopsy two perforations due to extreme thinning of the bowel wall were found; there was no evidence of obstruction. Meconium peritonitis — the name

given to peritoneal involvement secondary to intrauterine rupture of the intestinal tract — results from irritation produced by bile and other material. This condition may also be associated with pneumoperitoneum. If the rupture occurs before birth, there is no bacterial peritonitis. There is, however, evidence of meconium irritation of the serosal surfaces of the bowel. This may be demonstrated in the roentgenograms as calcification as well as grossly at operation. Perforations of the intestine, with leakage of intraluminal intestinal gas without gross peritonitis, have been reported in adults. This is attributed to a sealing-off process which Singer[3] has termed valvular pneumoperitoneum. In all these types of pneumoperitoneum the source of the primary lesion is usually apparent at operation if the correct diagnosis cannot be made preoperatively on clinical and x-ray examination.

There is also evidence that gas may find its way into the peritoneal cavity from the thorax. Hinkel,[4] in 1940, reviewed the literature and found 2 adult cases of spontaneous pneumoperitoneum without peritonitis. He reported a third case, that of a seventy-year-old woman, and suggested a possible temporary communication between aerated lung parenchyma and the peritoneal cavity, which, however, was not proved. Elrich[5] and others who have done extensive work with therapeutic pneumothorax pointed out that gas beneath the diaphragm rarely appears as a complication of this procedure. Sidel and Wolbarsht,[6] in 1944, reported a case of pneumoperitoneum in a sixty-three-year-old man discovered accidentally during the course of pneumonia that cleared in a month's time without therapy.

In the case reported above, as well as the 2 cases presented by Birdsong and Frame,[1] air from a ruptured alveolus may have escaped along the peribronchial tissues to the mediastinum. From here, conceivably, there could have been leakage into the peritoneal cavity around the structures in the diaphragmatic hiatuses. No gas was visualized, however, in the pleural cavity or mediastinum in the x-ray films, suggesting that the air reached the peritoneal cavity from some other source. At the present time the pathogenesis of these cases remains obscure. The term spontaneous pneumoperitoneum simply signifies no known etiologic process.

Symptoms and Signs

From the 3 reported cases, including the infant described above, the clinical findings of spontaneous pneumoperitoneum of the newborn consist of one or more of the following observations: lethargy, refusal of feedings, regurgitation, vomiting, respiratory distress, cyanosis, abdominal distention and diminished or absent peristalsis. The pathognomonic laboratory finding, however, is free air in the peritoneal cavity without associated signs of peritonitis or bowel obstruction as shown by roentgenologic studies.

Treatment

Birdsong and Frame[1] treated their second patient expectantly in spite of x-ray evidence of pneumoperitoneum discovered at twenty-four hours of age. The baby, who was given nothing by mouth, with continuous oxygen and antibiotics, recovered completely. Because of the rarity of this condition, if it does exist as an entity, compared with the frequent occurrence of pneumoperitoneum as a secondary phenomenon to visceral perforation requiring surgical correction, I believe that exploration should be carried out in all cases. Additional supportive measures should include gastric suction, oxygen as necessary, antibiotics and intravenous feedings until there is evidence that leakage from visceral rupture is absent. Postoperative x-ray studies at appropriate intervals to visualize any decrease or increase in intraperitoneal gas should help determine the therapy in the postoperative course. Complete absorption of the free air in the peritoneal cavity, with no associated mortality, was characteristic of these 3 cases.

Summary and Conclusions

Pneumoperitoneum in the newborn, with no demonstrable break in the gastrointestinal tract and not associated with obstruction or peritonitis, is an unusual occurrence. A case fulfilling these criteria is reported, and the pathology is discussed. It is suggested that the term "spontaneous pneumoperitoneum of the newborn" be given to this entity until the etiology becomes clarified. The clinical findings and treatment are briefly discussed.

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MEDICAL PROGRESS

THE MENOPAUSE*

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DESPITE a voluminous literature concerning the menopause, there are misconceptions and confusion about the significance and the proper management of this period in woman's life. Discussion continues regarding which of the symptoms associated with the menopause are due to hypoestrogenism and which are due to psychogenic factors, although several excellent reviews have been presented.[1-12] There is disagreement about the use of hormones in menopausal therapy. The nature of the advertising appearing in both medical and lay publications, the unfortunate practice of attributing any symptom arising in the middle-aged woman to the menopause and the misconceptions still passed from mother to daughter have all helped perpetuate many untruths. As long ago as 1897, Currier,[13] criticizing the work of Tilt on the menopause, wrote as follows:

> It has handed down the hoary tradition, which has been current from time immemorial among both the laity and the profession that the menopause is an experience fraught with peril and difficulty. This and all similar teaching the writer declares to be incorrect and unwarrantable in the light of his own experience and observation. . . [He] was never able to see the sense nor the logic of the traditional teaching, repeated generation after generation that the menopause was a serious — yea, even a most dangerous time and experience; and that the matron and the maid alike should approach it with fear and awe . . . .

It is the purpose of this paper to review the problem of the menopause and to indicate a rational approach to its management.

PHYSIOLOGY

The menopause appears to be an event unique in the human primate. Although lower animals experience decreased fertility, they are still capable of reproduction at advanced ages, and their ovarian follicles still contain ova.[14] Thoroughbred pedigreed mares, for example, have had viable colts while in their early twenties — an advanced age for a horse.[15] It has been suggested, with an admitted lack of reverence, that the menopause is a biologic accident and that women were perhaps not originally destined to live for as many years postmenopausally as modern medical science now permits.

The basic event is failure of ovarian function, manifested first by decreasing frequency of ovulation and later by decreasing production of estrogen. Although it was formerly believed that no estrogens were excreted after the menopause, observations on patients with high gonadotrophin titers and atrophy of the ovaries, uterus and vagina who responded to castration by development of menopausal symptoms suggested that the postmenopausal atrophic ovary may still be secreting small amounts of estrogen.[16] More recently, studies of excretion of urinary steroids indicate a decline in the total estrogen excreted from the third to the sixth decade but with a constant low level thereafter.[17] Paulsen et al.[18] have shown by studies of urinary excretion of estrogen that in many women the ovary continues to function at a low but significant level and in many cases can be stimulated by administered gonadotrophins.

It is generally stated that the menopause occurs, on an average, at the age of forty-seven but may begin at any time from forty to fifty-five. With ovarian failure, the menstrual periods may suddenly cease and become irregular, more profuse or less profuse, but eventually permanent amenorrhea occurs. Most observers consider it improper to make a diagnosis of menopause until menstrual function has ceased.

As estrogen activity diminishes, the pituitary gland enlarges, with an increase in cellular elements.[19] The urinary excretion of follicle-stimulating hormone rises. There is disagreement whether excretion of luteinizing hormone decreases[20] or increases,[21] but in the normal menopause, these are probably gradual changes.[22] Studies of follicle-stimulating-hormone excretion in women castrated surgically show a significant rise as early as the sixth to the tenth postoperative day. Hot flashes usually are apparent in a few days but, according to Heller et al.,[16] may be absent up to the twenty-seventh postoperative day.

The hot flash, the main symptom of the menopause, occurs most commonly under conditions in which heat production is increased, such as excitement, emotion, exercise and eating, or in which heat loss is impaired — that is, warm weather and heavy bed clothes. According to Albright,[23] the hot flash is mediated by elevated gonadotrophins and is not due primarily to hypoestrogenism. The basis for this thesis is that, after oöphorectomy, estrogen disappears long before hot flashes begin, that, during the menopause, the estrogen level can, by treatment, be raised above normal before hot flashes cease and that hypoestrogenism due to pituitary disease is not accompanied by hot flashes. There are, however, objections to the theory that excess gonadotrophins

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cause hot flashes. It can be shown that the use of amounts of estrogen too small to affect the titer of follicle-stimulating hormone will result in amelioration of symptoms,[24] and it has been observed that patients with ovarian agenesis and high levels of follicle-stimulating hormone do not have hot flashes till estrogen is administered and withdrawn.[25] Funnell, Keaty and Hellbaum[20] believe that at the time of the menopause, luteinizing hormone is not discharged from the pituitary gland and have shown that estrogen acts to release luteinizing hormone from the pituitary glands of menopausal women. Hellbaum, Eskridge and Payne[26] suggested that relief of vasomotor symptoms obtained from estrogen and androgen might be due to the stimulation of luteinizing-hormone release and found that the administration of luteinizing hormone benefited vasomotor symptoms in 4 patients. The logic of these observations is weakened by the work of those who find an increase rather than decrease of luteinizing hormone at the time of the menopause.[21,22]

The mechanism of the hot flash has been studied by Reynolds et al.,[27,28] who showed, by plethysmograph studies, that estrogens can produce a slow, progressive increase in finger size without change in skin temperature. This is called the plateau response. Superimposed on this response is a sharp increase in finger volume accompanied by an increase in skin temperature and termed the flash response. In the plateau response, blood vessels beyond arterioles are dilated, whereas the flush type, which is similar to the naturally occurring symptom, involves arteriolar dilatation. After treatment of menopausal women, the flush response diminishes in frequency. Of great significance was the observation[29] that in 10 of 13 patients with artificial menopause, it was possible to relate relief from menopausal flushes to the specific readjustment of some psychogenic, medical or social problem. The nature of the conditions under which hot flashes occur — namely, heat production increased or heat loss impaired, suggests that the menopausal woman is deficient in the mechanisms for heat loss or the centers of regulation of heat loss may be unduly sensitive to otherwise inadequate stimuli:

> It, therefore, follows that estrogen, sedatives or correction of neuroses, alone or combined with other therapeutic measures, may be effective in alleviation of the vasomotor menopausal disturbances through the action which they have in facilitating adequate and normal circulation of blood in the skin. The extent to which this is achieved by peripheral circulatory adjustments may be shown by suitable studies, whereas the central effects which therapeutic measures possess would appear to be at the level of the brain stem at which temperature regulating centers are located. This would point, therefore, to the hypothalamus as the seat or focus upon which psychogenic or other bodily influences play, directly or indirectly, with such mischief after surgical removal of the ovaries in women.[29]

With deficient estrogen stimulation, atrophic changes occur in the uterine endometrium.[30] The uterus shrinks, and the cervix becomes smaller. The vaginal epithelium becomes thin. McLaren[31] has reviewed in detail the genital changes, pointing out the great individual variation in vaginal histology that may be observed and suggesting that some ovarian activity may continue after the menopause. The ovary shows a gradual loss of primordial ova and progressive thinning of the cortex. The vessels of the hilus and medulla become progressively sclerosed.[32] Postmenopausally, production of the anabolic estrogenic hormones is decreased. Corticosteroid production continues at a less impaired rate, and the resulting effect is antianabolic, resulting in increased protein catabolism. The clinical effect, according to Albright,[33] is gradual attrition of skin and muscles and the development of osteoporosis.

Clinical Aspects

There is in the literature little information concerning the number of women who have sufficient symptoms at the time of the menopause to seek medical advice. A statistical study[34] of 1000 women in England indicated that 15.8 per cent had no symptoms at the time of the menopause, 62.3 per cent had only hot flashes for an average duration of two years, and 89.7 per cent carried on their daily activities without interruption. Although some have reported that as many as 75 per cent of women have distressful symptoms at the menopause,[35] it is more generally agreed that 10 to 15 per cent of women will present themselves for medical advice for symptoms attributed to the menopause.[8]

As defined, the menopause is the time in a woman's life when she ceases to menstruate and can no longer conceive. The term usually applies to the period of physical and psychologic adjustment that probably averages about two years in duration. It is commonly held that menopausal symptoms are more pronounced in those in whom ovarian function ceases abruptly, the severity depending on the rapidity of the aging process of the ovary.[36] It may be that there are two types of women: one with sudden and complete deprivation of estrogen and rapid regressive changes, and the other with amenorrhea also but with sufficient residual estrogen secretion to prevent significant symptoms.[37] It is stated that the menopause induced surgically or by radiation produces more severe symptoms.[2] Turnbull,[38] however, did not find much difference in symptoms between a group of women with normal menopause and a group with radiation-induced menopause. Novak[8] also does not believe that the surgically induced menopause is more severe than the normal, stating that the differences are due to variations in individual temperament.

It seems justified to distinguish the symptoms of the menopause from the postmenopausal clinical problems associated with atrophic changes of skin, muscle and bone. Greenblatt[39] has called attention to

the need for more emphasis on the attending metabolic disorders.

The only actual symptoms resulting from diminished ovarian activity are amenorrhea and vasomotor instability as manifested by hot flashes, and even the hot flashes, although clearly mediated hormonally, can be greatly alleviated by simple reassurance. The flush is usually described as a sudden feeling of heat in the face, neck and chest, associated with diffuse or patchy flushing of the skin, and perspiration. In some, there is only the feeling of heat without flushing or perspiration.[7] Such episodes are called hot flashes by some. In common usage, however, the terms hot flush and hot flash are usually not so finely distinguished. It is not commonly appreciated that the flush may be followed by a sensation of chilliness. The host of other symptoms, such as irritability, palpitation, dizziness, paresthesias, emotional instability, depression, insomnia, fatigue, jealousies and self-depreciation, that are listed as components of the "menopausal syndrome" are manifestations of the psychologic disturbances that may appear at this time of life. There is no evidence that the symptoms of anxiety and depression are causally related to estrogen lack, nor is there proof that estrogen administration helps alleviate any symptom other than the hot flash. These statements have been made in so many previous writings that to refer to them is superfluous. Yet, even today, most women, including the most enlightened, expect to undergo at the menopause one or more of these symptoms. There is evidence that the dread and fear with which many women in civilized groups approach the menopause is not so prevalent in more primitive societies, where, in general, there is respect for old age and where, in many groups, previous taboos are lifted as the menopause occurs. The grounds for granting increased privileges at this time vary in different tribes but are frequently based on the belief that the change of life builds up protective virtues or immunities against dangerous objects or practices. Numerous examples of the increased privileges and freedom of women in the menopause are recorded by Simmons.[40]

Much of the advertising appearing in the lay press does nothing to dispel the erroneous concepts that many women hold. The amount of misinformation passed from mother to daughter or obtained from well meaning friends is appalling. A public educational campaign could do much to relieve the misconceptions regarding the menopause. It is clear that a major portion of the physician's duties is to educate the menopausal patient in the nature of the phenomena. This idea has been well expressed by Friedlander.[41] Even more tragic is the tendency among both patients and the medical profession to regard all symptoms of middle life as being due to the menopause and, therefore, not being worthy of investigation. Thus, patients may then disregard a symptom of serious disease or may report to the physician asking for "change-of-life shots." The physician who assumes the symptoms to be menopausal in origin and who fails, therefore, to obtain a careful history and do a physical examination, which should always include a pelvic examination, does a great disservice to his patient. There is also an unfortunate tendency for advertisements appearing in the medical journals to leave the physician with the concept that his only problem is the selection of the proper hormonal therapy.

Psychologic Problems

The symptoms of the menopause that are most troublesome and send patients to their physicians are usually not related to diminished estrogen production but to the psychologic conflicts of middle age. English,[42] as well as many others,[1-6,43-47] has discussed the more common problems that beset the woman in middle life.

It is at about middle age that a woman finds her role in the family circle undergoing a change. Her children are either adolescent or full grown, with interests developing outside the family circle, creating in her a sense that she is no longer needed. She may have failed to fulfill social aspirations for herself or her family, or she may have suffered disappointment in her children. The loss of ability to reproduce may create the feeling that her useful years are at an end. She has probably been led to the erroneous belief that she can expect loss of libido and that her attractiveness to her husband will be lost. Fears of insanity, obesity or cancer may beset her. She is, in a sense, forced to retire from her primary activity of caring for her children. Her activities are in contrast to those of her husband, who at this time is usually at the peak of his energies in his business or profession.

It is easy to see that these conflicts, for which most women have been poorly prepared, result in anxieties and depressions. Whether or not a woman will have psychoneurotic symptoms can be generally correlated with her previous response to emotional problems. If she has not had a psychoneurotic episode before, she is not likely to have one at the menopause.[48] Women with a long history of dysmenorrhea are likely to have a difficult menopause.[34] Numerous studies[48-51] have indicated clearly that the symptoms of anxiety and depression can be related to pre-existing emotional disorders that are brought to light or exaggerated by the situational stress occurring at the time of the menopause. In Donovan's[52] series of 110 patients with menopausal symptoms, 95 per cent had a past history of an unusual number of somatic symptoms unexplained by organic disease and antedating the menopause by decades. Pain perception and the pain-reaction thresholds of menopausal women are similar to those of psychoneurotic patients.[53]

It is held that a group of psychoses occurring at the time of the menopause can be recognized as a distinct reaction type representing a failure in adjustment to the problems specific to that age of life.[54] The climacteric is involved, but these disorders should not be considered entirely due to physiologic changes. The development of a psychosis depends upon special types of personality organization lacking in plasticity and restricted in interests, conditioning experiences, which enhance these weaknesses, and precipitating factors that threaten the sense of security. Some confusion exists about the terms involutional psychosis and involutional melancholia. The latter is frequently applied to menopausal depression and by most is considered to be related to the psychosis only in degree of severity. Wright,[55] however, objects to the use of the term involutional melancholia to imply that a particular kind of psychopathy is the product of a hormonal disturbance or of the specific problems with which the patient has to deal in the involutional period.

It should, at this point, be re-emphasized that the anxieties and depressions do not affect the majority of climacteric women and that, as Novak[10] has pointed out, in many women the menopause comes as a boon, with striking improvement in general health and well-being apart from the elimination of the physical and mental stress of child raising.

The majority of students of the menopause stress the fact that the proper approach is explanation, reassurance and simple psychotherapy.[56] Both Ross[57] and Weed[58] have again claimed that the great majority of patients do not need hormonal therapy and that the mere correction of hormonal imbalance may fall far short of effective treatment. Considerable relief can be afforded if the patient discusses her symptoms with a physician who is willing to listen. Only a few hold that the anxiety and depressive features will respond to estrogen administration.[59,60]

As generally accepted, the menopause does not occur until periods have ceased; yet it is not uncommon for women still menstruating to complain of hot flashes and anxiety symptoms. Although the hot flashes occurring in this situation could be explained on the basis of anxiety there is evidence that elevation of gonadotrophin titers[61] and decreased estrogen production precede cessation of menstruation. Sauramo[62] has shown that involutional changes in the ovary occur before the menopause. According to Howard et al.,[63] there is a period during which gonadal failure is met by overproduction of follicle-stimulating hormone, with preservation of gonadal function. This has been called the "compensated menopause." In a short while, gonadal failure is not counterbalanced in spite of increased production of follicle-stimulating hormone, and gonadal failure becomes demonstrable clinically.

Clinical Conditions Related to the Menopause

In view of the fact that the menopause occurs at a time of life when there is a rising incidence of degenerative disease, it is perhaps not surprising that a causal relation between some of these disorders and the menopause should have been postulated.

Cardiovascular

For a time, it was alleged that some cases of hypertension were caused by the menopause, and the term menopausal hypertension was in common use. In 1935, a report appeared describing 13 patients in whom estrogen administration coincided with lowering of blood pressure, a causal relation being inferred.[64] However, Taylor, Corcoran and Page,[65] in a study of 179 ovariectomized women and 21 women with natural menopause, observed before and after the menopause, found no increase in the prevalence of hypertension over that occurring in the general population, and it has been generally agreed that hypertension at the menopause is not hormonally mediated. Recently, however, a beneficial effect of estrogen on hypertension has again been suggested.[66] It was reported that in 52 cases of hypertension, a lowered blood pressure followed the administration of estrogen, or a combination of estrogen and androgen with calcium. Simultaneously, many of the patients received moderate doses of sedatives so that evaluation of the results is difficult.

Currently, a great deal of interest is being centered on the disparity in the average degree of coronary atherosclerosis between men and women of comparable ages. It is postulated that an ovarian hormonal factor is responsible for the delay in the development of atherosclerosis in women as compared to men. Wuest, Dry and Edwards[67] demonstrated that the degree of arteriosclerosis in women subjected to bilateral oöphorectomy was greater than that in control women but less than that in control men.

Recent work[68] has shown that in cholesterol-fed chicks, estrogens can inhibit the development of coronary atherosclerosis and can cause regression of established atherosclerosis.[69]

A significantly higher ratio of cholesterol to phospholipids has been demonstrated in the serum of patients with known coronary atherosclerosis than in a normal control group.[70] There is, in normal persons, a tendency for serum cholesterol to rise with age and to be accompanied by a comparable rise in phospholipids. In patients with coronary atherosclerosis, phospholipids fail to rise as rapidly with age, resulting in a higher ratio of cholesterol to phospholipid.[71] It is believed that this higher ratio encourages the development of atherosclerosis and that a low ratio is more protective against the development of atherosclerosis.

Oliver and Boyd[72] found a fall in plasma cholesterol ester, a less marked fall in plasma phospholipids and, therefore, a decrease in the total cholesterol phospholipid ratio at the time of ovulation and immediately before menstruation — points in the menstrual cycle when estrogen activity is highest. Eilert[73,74] and Oliver and Boyd[75] have demonstrated that estrogens can produce a sharp reduction in the ratio of total cholesterol to phospholipids. The ratio is changed by a fall in serum cholesterol with the phospholipid pattern remaining constant or by both a fall in cholesterol and an increase in phospholipid. These observations suggest that estrogen with its beneficial effect on this ratio may be a factor in the lower prevalence of arteriosclerosis in women. Oliver and Boyd[76] have also demonstrated a significant elevation of the ratio of plasma total cholesterol to cholesterol phospholipid in patients with coronary atherosclerosis at all ages and in both sexes, with the exception of the sixth decade in women. At the sixth decade in women, the ratio of mean plasma cholesterol to mean plasma total cholesterol phospholipid in a control group rose to levels similar to those in patients with coronary atherosclerosis. Russ, Eder and Barr[77] found that the cholesterol-phospholipid ratio of the fraction of plasma containing alpha lipoproteins averaged 0.5 whereas the fraction containing the beta lipoproteins had an average ratio more than twice as great. The plasma of young women between eighteen and thirty-five years of age contained more alpha and less beta lipoprotein than that of men of comparable age. Normal men and women between the ages of forty-five and sixty-five did not exhibit this sex difference. Barr[78] states that estrogen can produce an increase in percentage of cholesterol in alpha lipoprotein and a decrease in percentage of cholesterol in beta lipoprotein.

The possible relation of these observations to the beneficial effect of estrogens is obvious, and an argument can be made in favor of prolonged postmenopausal estrogen administration on the basis of these observations.

Arthritis

For years the question has been debated whether the arthritic disorders occurring at the time of the menopause are a specific entity and related to hypoovarianism. Joint symptoms occur in about 23.7 per cent of women at the time of the menopause[84] and are five times more common in women than men in a comparable age group.[79] The concept of a villous or climacteric arthritis, distinguished in no clearly definable way from hypertrophic or rheumatoid arthritis, has arisen.[80] The condition is said to be the result of hypertrophy and proliferation of normal fatty synovial villous fringes, and the pain to be due to chronic strain of weakened ligaments and muscles.[81] Climacteric arthritis is supposed to produce symptoms chiefly in the knees and to be associated with obesity and flat feet.[82] Hall[79] reviewed the literature and pointed out that there are those who believe that the menopause merely makes women more susceptible to arthritis but that endocrine dysfunction is not the cause of arthritis. He refers to others who hold that there is a clear type of hypertrophic menopausal arthritis, and still others who believe that estrogen deficiency is responsible for various patterns of arthritis, as well as arthralgia and rheumatoid and hypertrophic arthritis. He studied 71 patients with joint symptoms after castration, 53 of whom had arthralgia rather than true arthritis. Forty of these were treated with estrogen, and 80 per cent were materially relieved of joint symptoms. Of 18 patients with true arthritis, 50 per cent seemed to benefit from estrogen administration. Hall concluded that an arthralgia is associated with the menopause but that the existence of true menopausal arthritis remains unproved. Greenblatt and Kupperman,[83] in 1946, stated that the symptoms of menopausal arthralgia and arthritis may be ameliorated by estrogenic therapy. At present it is fair to state that the arthralgias at the time of the menopause seem to be relieved by estrogens but that there is still no conclusive evidence of an arthritis caused by estrogen deficiency. There is evidence that Heberden's nodes appear at the time of the menopause,[84] perhaps because of alterations in peripheral circulation but without proof of any other causal relation.

Menstrual Abnormalities

With failure of ovulation and decreasing production of estrogen, one of the more common problems of the menopausal patient is abnormal uterine bleeding. The menses may suddenly cease without warning. There may be decreasing frequency or duration of periods or excessive and prolonged bleeding. Almost any variant of abnormal bleeding may occur at the time of the menopause, probably because of wavering titers of estrogen and a deficiency of progesterone. The situation calls for nice judgment about when to advise curettage to eliminate the ever-present possibility of uterine cancer. In general, recurrence of bleeding after a lapse of six months, prolonged spotting or marked prolongation of periods are situations warranting dilatation and curettage, but, increasingly, the problem of the management of abnormal bleeding at the menopause is complicated by previous injudicious administration of estrogens, which have produced bleeding.[85] Randall[86] claims that when postmenopausal bleeding occurs, the chance that cancer has developed is three and a half times greater in the woman with a history of menorrhagia during the climacteric than in the woman who did not experience increased bleeding before her periods ceased.

Miscellaneous Clinical Conditions

A peculiar form of muscular dystrophy, occurring at the time of the menopause and consisting of progressive weakness of hip and shoulder-girdle muscles, has been reported by Shy and McEachern[87] and called by them menopausal muscular dystrophy. It has not been shown to be due to estrogen lack, however, and cases have been reported in males.[88]

Hepatitis, in some epidemics, seems to have a higher incidence and a higher mortality in menopausal women.[89] No explanation of this peculiarity has been offered.

It is of interest that diabetes occurring before and during the menopause has been shown to be ameliorated by estrogen administration.[90,91] It has been suggested that this effect is due to suppression of growth-hormone production by the pituitary gland.[92] It has also been suggested that the symptoms of thyrotoxicosis occurring in women at the time of the menopause are due to overactivity of the pituitary gland. In a series reported by Branwood,[93] the disorder did not respond to thiouracil but was controlled by stilbestrol. Such observations suggest the unlikely possibility that diabetes and hyperthyroidism of pituitary origin occur in menopausal women, with estrogen acting to suppress pituitary hormones other than gonadotrophins, but further confirmation is needed.

Migraine is said to decrease in severity and frequency at the time of the menopause, and yet Alvarez[94] found that only 6 of 42 patients with induced menopause were relieved of their headaches. Ziskin and Moulton[95] have described oral symptoms in menopausal women. Common complaints may be burning, itching, stinging, dryness and a bad taste or sensation of sand in the mouth. The symptoms may seem to arise from the throat or floor of the mouth. Such symptoms are most likely to occur in postmenopausal women, usually without visible lesions. Estrogens usually do not relieve the symptoms although systemic effect can be shown by oral and vaginal smears. The authors conclude that orolingual pain is primarily a psychogenic symptom in menopausal women who suffer from emotional conflict, sexual maladjustment or cancerphobia.

Allergic rhinitis, according to Lucas and Pepys,[96] may be associated with the menopause. These authors described 57 patients with allergic rhinitis whose symptoms began in relation to the menopause or were aggravated at that time. Treatment with estrogens alone resulted in benefit to 33 of the 57 patients. It was concluded that, in this group, the endocrine disturbance of the menopause made manifest a latent or subclinical allergic state or aggravated a previously existing allergic condition.

A new physical sign of the climacteric, tenderness of the lower third of the tibia anteriorly, was reported by Traut[97] in 77 per cent of women with menopausal amenorrhea. This sign was not observed in menstruating women or in those with amenorrhea not due to the menopause. It was found in 3 men, of whom 2 were sixty-six and 1 seventy-two years of age.

It is not widely appreciated that the atrophic changes occurring in the skin and vagina also take place in the urinary system. Urinary frequency and burning may result from atrophy of the urethral meatus, and a latent cystocele and rectocele may become more noticeable.[98] Greenblatt[36,39] recently called attention again to the significance of urinary-tract symptoms in the postmenopausal woman and commented on the improved tonus of urinary-bladder musculature and sphincter after androgen and estrogens are administered.

Of several disorders of the skin that are more frequent at the time of the menopause, keratoderma climactericum is often mentioned.[99-101] In this disease, hyperkeratotic plaques with erythematous bases occur on the palms and the soles. The condition appears to be helped by estrogen treatment. Although it is most commonly seen at the menopause, it may occur in young women. Seborrheic keratoses and eruptions tend to develop at the menopause and are reportedly helped by estrogen. Neurodermatitis, which usually appears at the nape of the neck, vulva, pubic region and groins, and psoriasis are more common at the climacteric. Swelling of the eyelids is also mentioned, and an ocular syndrome consisting of burning, smarting, dryness, irritation and mild photophobia has been described.[102] It is suggested that change in the composition and the amount of tears from lacrimal-gland atrophy may account for the symptoms. Of 53 patients studied, all responded to estrogen.

Postmenopausal Disorders

The major postmenopausal changes of clinical importance concern the skin, genital tract and bones. Gradual loss of vulvar fat and pubic hair occurs, and thinning of the vaginal epithelium that sometimes leads to senile vaginitis. The response of vaginal mucosa to estrogen administration is well known to clinicians, and Goldzieher[103] has neatly demonstrated the effect of topical application of estrogens on restoring senile skin to normalcy. Post-treatment skin biopsies in aged women showed regeneration of atrophic epidermis and comparable changes in the structure of the cutis, including regeneration of elastic fibrils. Palmer[104] recently reviewed the dermatologic problems of aging women.

Of great and increasing importance is the problem of osteoporosis. Albright, Bloomberg and Smith,[105] in 1940, first pointed out the association of the postmenopausal state and osteoporosis and demonstrated that estrogen could produce positive calcium and phosphorus balance in such women. Kyes and Potter[106] showed that the bones of male doves are osteo-

porotic as compared with those of female doves, in which cyclic ossification of the red marrow of the long bones of the leg coincides with maturing of the ovarian follicle. Pfeiffer and Gardner[107] demonstrated that in pigeons, estrogen administration is followed by an increase in serum calcium similar to that occurring normally at the time of ovulation. These observations provided the rationale for the study of effects of estrogen in women with postmenopausal osteoporosis. Subsequently, in 1941, Albright, Smith and Richardson[108] reported further on the clinical features. They indicated that in osteoporosis there is deficient bone formation because the osteoblasts do not lay down sufficient osseous matrix. The serum phosphatase level, which is an index of osteoblastic activity, is not elevated, presumably because of hypoplasia of osteoblasts. The serum calcium and phosphorus levels are normal. Early in the development of osteoporosis the urinary excretion of calcium and phosphorus may increase. However, once the skeleton is depleted, urinary excretion of calcium and phosphorus is low. Clinically, the usual picture is that of a woman ten or more years after the menopause who complains of back pain frequently after a minor traumatic episode. X-ray examination demonstrates rarefaction of bone involving chiefly the spine and pelvis. There may be fractured or crushed vertebras, the so-called fish vertebras, or herniation of the nucleus pulposus through the end plates of the vertebras. The skull is rarely involved — an important point in differentiation from hyperparathyroidism, in which the skull is one of the first bones to show involvement. Obviously, other causes of osteoporosis, such as multiple myeloma and metastatic cancer, must be excluded.

According to Albright,[83] the adrenal S hormone is antianabolic and tends to decrease bone mass. The combined action of the adrenal N hormone, estrogens and androgens counteracts this effect, and a state of balance exists. At the time of the menopause, with decreasing estrogen production, the balance shifts in favor of the antianabolic hormones, and increased protein catabolism results. The observations of Heller and Shipley,[109] who showed a sustained secretion of corticoids in the presence of a decline in androgens, lends support to this thesis. Estrogen tends to restore this balance, to stimulate osteoblastic activity and to promote calcium retention for deposition in newly formed osseous matrix.[38,110-112] Clinically, estrogen is effective in relieving the pain associated with osteoporosis.[113] Excellent reviews on postmenopausal osteoporosis and senile osteoporosis have recently been published.[114,115]

(To be concluded)

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MEDICAL INTELLIGENCE

COMPARISON OF RAPID INTRAVENOUSLY AND ORALLY ADMINISTERED CONTRAST MEDIUMS FOR ROUTINE GALL-BLADDER STUDY*

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THIS study was initiated to determine the comparative effectiveness of intravenously administered and orally administered cholecystographic mediums for routine use in x-ray examination of the gall bladder. The recent introduction of iodipamide (disodium N,N-adipyl-bis [3 amino-2,4,6-triiodobenzoate]) solution, 20 per cent iodipamide sodium¶ for nonoperative choledochography and cholecystography stimulated our interest in the use of this substance for routine gall-bladder visualization. No attempt was made to evaluate the applicability of iodipamide for examination of the extrahepatic biliary ducts since this has been discussed in other communications.[1-3]

METHODS AND MATERIALS

The 68 cases studied in this series were selected at random, the patients having been referred to the X-Ray Department for routine oral cholecystography. All patients were suspected, from a clinical standpoint, of having gall-bladder disease. No patient presenting evidence of jaundice was included in this series.

All patients studied by the oral method were subjected to intravenous cholecystography, either immediately or within an interval of a week. When the intravenous method afforded visualization on the same day that nonvisualization of the gall bladder was obtained with the use of iopanoic acid,‖ an additional intravenous examination was performed after an interval of not less than a week to exclude the possibility of an additive or "boosting" effect from the previously administered iopanoic acid. No such additive effect was encountered.

X-ray study of the gall bladder with the orally administered contrast material was performed according to accepted technics. The patient was instructed to ingest 6 tablets (3.0 gm.) of iopanoic acid on the evening before the scheduled x-ray examination. The routine study included exposures obtained with the patient in the prone, erect and lateral decubitus positions, both before and after administration of a fatty meal (eggnog). Nonvisualization or poor visualization of the gall bladder was always followed by administration of a second dose of the oral contrast substance, with a repeated examination on the following day.

Preparation of patients for examination with iodipamide was essentially the same as that for oral cholecystography so far as dietary restriction and bowel cleansing were concerned. The omission of breakfast did not appear necessary if the examination was scheduled for the afternoon hours.

The technic of administration consisted in the introduction of 20 ml. of the 40 per cent intravenous solution injected slowly over a period of eight to ten minutes. This had been preceded by a preliminary test dose of 1 ml. of the iodipamide solution for detection of any undue reaction. A ten-minute interval was permitted to elapse before the injection was resumed.

The reaction to intravenous administration of iodipamide has been recognized in several previous articles.[1-4] Our experience has been in keeping with these reports, in that a low but appreciable number of patient reactions, consisting primarily of transient episodes of nausea, were encountered.

Although opacification of the biliary ducts occurred ten or fifteen minutes after injection, optimum gall-bladder visualization was obtained after an hour. When the gall bladder was not visualized, a two-hour x-ray observation was routinely employed. In several cases a twenty-four-hour delayed roentgenogram was obtained after a nonvisualization, and, on occasion, additional information was provided.

RESULTS

A total of 68 symptomatic patients were studied with both orally and intravenously administered cholecystographic mediums (Table 1). Twenty-four, or 35.3 per cent of the total number studied, exhibited satisfactory gall-bladder visualization after oral administration of the iopanoic acid. Of this group of 24 cases, calculus formation was observed in 10 (41.7 per cent).

When the same patients were examined by intravenous administration of iodipamide, the gall bladder was visualized in 39, or 57.4 per cent, of the total cases examined. Twenty-three, or 58.9 per cent, of the 39 studies demonstrated calculi.

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¶Kindly supplied as Cholografin by E. R. Squibb and Sons, New York City.

‖Available, as Telepaque, from Winthrop Laboratories, New York City.

Conversely, there were 44 cases, or 64.7 per cent, in which the gall bladder was not visualized with the orally administered cholecystographic medium, as compared to 29 cases, or 42.7 per cent, with the intravenous method.

There was only 1 case in which a gall bladder that was not visualized with the intravenous method was visualized with subsequent use of the oral method. This gall bladder, incidentally, contained several nonopaque calculi. In every other case of gall-bladder visualization with the orally administered medium, identical or superior visualization was obtained by the intravenous administration of dye.

Discussion

These results indicate a larger number and greater intensity of gall-bladder opacification with examination performed by the intravenous method using iodipamide. In a significant number of cases, nonopaque calculi were demonstrated in gall bladders previously classified as "nonfunctioning" after oral cholecystography.

Table 1. *Results in 68 Cases in Which Both Oral and Intravenous Cholecystography Was Performed.*

Result	Oral Method*	Intravenous Method†
	no. of cases	no. of cases
Normal gall-bladder visualization	14 (20.6%)	16 (23.5%)
Gall-bladder visualization with stones	10 (14.7%)	23 (33.8%)
Nonvisualization of gall bladder	44 (64.7%)	29 (42.7%)
Totals	68	68

*Iopanoic acid.
†Iodipamide.

Despite the apparent advantages of the intravenous method, the study showed that, for routine purposes, the oral administration of the radiopaque substance had certain benefits. The smaller number of reactions, the time-saving factor, both to patient and to physician, the necessity for less detailed supervision by the radiologist, the greater ease of administration of the material and the lower expense associated with oral cholecystography constituted sufficient reason not to use iodipamide for routine study.

Despite the few reactions to iodipamide, nausea or vomiting and an episode simulating peripheral vasomotor collapse were sufficiently dramatic to warrant caution in the use of this drug as a routine measure. This point should be stressed. To our knowledge no deaths have occurred with the use of this material. Complete evaluation, however, as with any intravenous medication, must await more extensive clinical application. We have revised our original estimate of the frequency and severity of untoward reactions.[4] Our regard for the merit of this material is tempered by a sound respect for the occasional reaction encountered.

The time required by the radiologist for the initial test dose, for the seven-minute to ten-minute final injection and for supervision of the technical aspects of the x-ray examination over a period of two or three hours is in strong contrast to the ease and simplicity of routine oral cholecystography.

Although intravenous cholecystography as a routine method of gall-bladder examination is not advocated, this method has proved of great value in selected cases requiring study beyond that afforded by the oral method. The introduction of iodipamide has necessitated the reappraisal of the frequently used designation of "nonfunctioning gall bladder." In this relatively small series of cases alone, 15, or 22 per cent, of the gall bladders examined were visualized satisfactorily with the intravenous method after nonvisualization with the oral method; in 12 of these cases nonopaque calculi were demonstrated. In properly selected nonjaundiced patients, the use of iodipamide appreciably increases the accuracy of x-ray diagnosis of the nonfunctioning or dysfunctioning gall bladder. Visualization by this means after oral cholecystography has failed to opacify the viscus affords a nonsurgical method of investigating the high percentage of "nonfunctioning" gall bladders reputed to contain nonopaque calculi.[5,6] It is believed that iodipamide can be used most efficiently as a cholecystographic medium in cases in which oral technics have failed. The inconvenience of an additional diagnostic procedure and the added cost to the patient are offset by the additional information to be obtained for aid in determination of definitive treatment.

Summary

Gall-bladder examination was completed in a total of 68 cases by means of both oral and intravenous cholecystography. Though a more satisfactory visualization was obtained by means of the intravenous method, oral cholecystography was deemed superior as a *routine* measure because of the greater ease and safety in performance of the examination. Intravenous cholecystography proved to be of great value in cases in which gall-bladder visualization was poor or absent after oral administration of the opaque material.

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CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

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CASE 42151

PRESENTATION OF CASE

First admission. A seventy-year-old man entered the hospital because of pain in the chest.

About an hour and a half previously the patient was awakened by severe aching substernal pain that radiated to the left arm. The pain was associated with dyspnea and nausea and was not relieved by nitroglycerin. An irregular cardiac rhythm was noted by his physician, who gave him an injection that relieved the pain.

A "leaky valve" was said to have been present for twenty-six years. For twenty-five years before entry the patient had episodes of substernal tightness with pain radiating down the left arm. These episodes occurred a few times weekly until the year before admission, when he avoided precipitating factors such as exertion or cold weather. Nitroglycerin, which had not been necessary for two or three months before entry, relieved the symptoms.

Occasional episodes of ankle edema had been noted several years before admission. Thirty-five years before admission he had pneumonia without sequelae. He smoked 40 cigarettes daily. There was no history of orthopnea, paroxysmal nocturnal dyspnea, palpitations, rheumatic fever, scarlet fever, hypertension or diabetes mellitus. He had taken digitalis twenty-five years previously for one year.

Physical examination showed a well nourished man in no distress. The neck veins were distended midway to the jaw when the patient was raised 30°. Examination of the chest showed emphysema and hyperresonance with a few crackling rales at both lung bases. The heart was enlarged to the left, with sounds of good quality and an irregular rhythm; the second aortic sound was slightly less than the pulmonic. There was a Grade 2 to 3 systolic murmur that was best heard over the aortic area and the fourth intercostal space along the left sternal border; it was transmitted to the neck. No friction rub or gallop was heard. The liver edge, which was nontender, was palpable 1 cm. below the right costal margin. There was no edema.

The temperature was 99°F., the pulse 156 and irregular, and the respirations 16. The blood pressure was 80 systolic, 50 diastolic.

The urine gave a +++ test for albumin; the sediment contained 20 red cells, 11 white cells and many hyaline and occasionally finely granular casts per high-power field. Examination of the blood revealed a hemoglobin of 13 gm. per 100 ml. and a white-cell count of 10,900, with 98 per cent neutrophils. The erythrocyte sedimentation rate was 45 mm. per hour. The nonprotein nitrogen was 45 mg., and the fasting blood glucose 128 mg. per 100 ml. The prothrombin content was normal. The blood Hinton test was negative. X-ray films of the chest on the fourth hospital day (Fig. 1) demonstrated enlargement of the heart in the region of the left ventricle; there also appeared to be some fullness of the left atrium. There was a suggestion of intracardiac calcification in the region of the mitral valve. The pulmonary vessels were somewhat full at the lung roots. An electrocardiogram showed atrial fibrillation with a ventricular rate averaging 120 and with frequent ectopic beats or aberrant conduction. The ST segments were depressed in Leads 1, 2, 3, aVL, aVF, V_5 and V_6; the T waves were inverted in Leads 1, 2, aVL, V_5 and V_6 and upright in Leads 3, aVF and V_1 through V_4; the R waves were absent in Lead V_1; high-voltage R waves were seen in Leads V_5 and V_6.

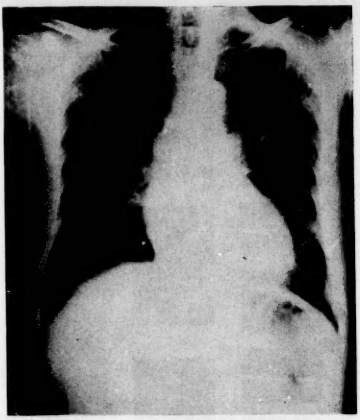

FIGURE 1. *Posteroanterior Film of the Chest, Showing Prominence of the Left Ventricle and Clear Lung Fields.*

With bed rest and digitalization the patient remained asymptomatic and afebrile. The blood pressure gradually rose to 150 systolic, 60 diastolic. By the day after admission the pulse was regular at a

rate of 72, and the neck veins were no longer dilated. The white-cell count was 9100. The sedimentation rate was 12 mm. per hour. An electrocardiogram showed a normal rhythm at a rate of 75, a PR interval of 0.20 second and a normal axis. The ST segments were depressed in Leads 1, 2, 3, aVL and aVF; the T waves were inverted in Leads 1, aVL and V_4 through V_6, diphasic in Lead 2 and upright in Leads 3, aVF, and V_1 through V_3; the ST segments were elevated in Leads V_1 through V_3 and depressed in Leads V_4 through V_6; R waves were absent in

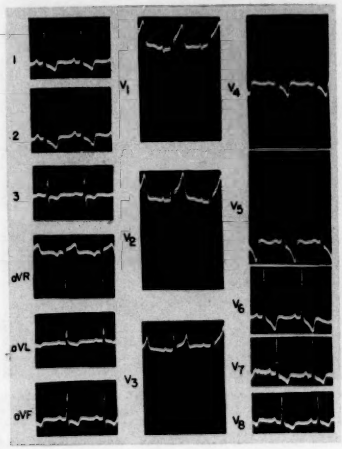

FIGURE 2. *Electrocardiogram.*

Lead V_1; high-voltage R waves were present in Leads V_4 through V_6. On the second hospital day the white-cell count was 14,500, with 82 per cent neutrophils. The erythrocyte sedimentation rate was 20 mm. per hour. The serum nonprotein nitrogen was 70 mg., the calcium 9.1 mg., the phosphorus 3.7 mg., and the fasting blood glucose 89 mg. per 100 ml. The serum sodium, chloride and potassium were normal. An electrocardiogram on the third hospital day revealed a normal rhythm at a rate of 75 and a PR interval of 0.16 second. The T waves were inverted in Lead 1 and in Leads V_4 through V_6 and diphasic in Leads 2 and 3 and upright in Leads V_1 through V_3. There were enormous-voltage QRS complexes over the left side of the precordium. The patient was gradually ambulated beginning on the eighth hospital day. At this time the white-cell count was 7700, and the sedimentation rate was 33 mm. per hour. A phenolsulfonphthalein test showed 25 per cent excretion of the dye in fifteen minutes and 65 per cent in two hours. Because of a persistently elevated serum nonprotein nitrogen a cystoscopy was performed on the seventeenth hospital day. A moderate degree of urethral obstruction from an enlarged prostate was seen. Retrograde pyelograms were normal except that the left kidney was slightly smaller than normal. Two days after the cystoscopy the temperature rose to 101.6°F. Several hours later there was a half-hour episode of precordial pain that was relieved by codeine. Culture of the urine showed abundant coliform bacilli. Blood cultures showed no growth. With antibiotic therapy and catheter drainage of the urinary bladder the temperature returned to normal, and the serum nonprotein nitrogen fell to 34 mg. per 100 ml. An electrocardiogram on the twenty-second hospital day showed a normal rhythm at a rate of 75; deep inversion of the T waves in Leads 1, 2 and V_4 through V_8; slight sagging of the ST segment in Lead 3; wide amplitude of the QRS complexes, especially in the precordial leads; and deep S waves over the right side and high R waves over the left side of the chest. There were no abnormal Q waves (Fig. 2). The patient was discharged on the thirty-second hospital day.

Final admission (three months later). In the interval the patient was asymptomatic except for a rare episode of substernal pain relieved by nitroglycerin. Two days before entry there was a sudden onset of severe substernal pain lasting for five hours and associated with sweating, weakness and an irregular cardiac rhythm. The pain was relieved by an injection. With quinidine therapy the rhythm reverted to normal. During the night before admission the patient noted shortness of breath that was relieved by morphine intravenously. On the morning of the day of admission he was awakened by severe pain under the sternum, and in the left side of the chest anteriorly, that was not relieved by morphine. There was associated pallor, sweating, shortness of breath and vomiting.

Physical examination showed a slightly cyanotic man in moderate respiratory distress and complaining of dull chest pain. The neck veins were full with the patient lying flat in bed. Examination of the chest revealed moist inspiratory rales over both lung bases up to the level of the scapula. The heart was enlarged, its border extending 3 cm. to the left of the midclavicular line. The rhythm was regular, with a protodiastolic gallop heard at the left sternal border. The second aortic and pulmonic sounds were equal. A Grade 2 aortic systolic murmur that was transmitted to the neck and a blowing Grade 3 apical systolic murmur were audible. The liver edge, which was firm and nontender, was palpable 4 cm. below the right costal margin. There was no ankle edema.

The temperature was 98.6°F., the pulse 90, and the respirations 20. The blood pressure was 125 systolic, 70 diastolic.

Examination of the blood revealed a hemoglobin of 11.6 gm. per 100 ml. and a white-cell count of 16,900, with 71 per cent neutrophils. The sedimentation rate was 50 mm. per hour. The serum nonprotein nitrogen was 48 mg., and the fasting blood

sugar 100 mg. per 100 ml. The serum sodium, potassium, carbon dioxide and chloride were normal. The serum transaminase on the fourth hospital day was 31 units. The prothrombin content was 67 per cent. The urine gave a + test for albumin; the sediment contained 1 red cell and 40 white cells per high-power field. An x-ray film of the chest on the eighth hospital day demonstrated further cardiac enlargement since the previous films (Fig. 3); there were bilateral congestive pulmonary changes, with a moderate pleural effusion at the right-lung base.

Therapy included bed rest, digitalis, quinidine, oxygen, morphine, aminophylline, Mercuhydrin and Gantrisin. On the day of admission a persistent, loud friction rub became audible over the entire precordium. A systolic component could be heard in all areas; a short early diastolic component was heard near the apex. The protodiastolic gallop was greatly accentuated. The pulse became regular at a rate of 80. On the first hospital day there was still a residual substernal ache that later subsided. The gallop rhythm disappeared; 900 mg. of Tromexan was given. During the next day the temperature rose to 100.2°F. and ranged between normal and 99.6°F. during the next four days; thereafter it was normal. On the second hospital day there was a decrease in the pulmonary rales. The patient was given 150 mg. of Tromexan and 50 mg. of Dicumarol. The prothrombin content was 21 per cent. There were episodes of delusions and hallucinations. An electrocardiogram showed uncontrolled atrial fibrillation at a rate of about 160; the QRS interval was 0.06 second; the ST segments were sagging and the T waves were diphasic in Leads 1, 2, aVL and aVF; the ST segment was markedly depressed, and the T waves were diphasic in Leads V_4 through V_6; there were deep S waves in the right precordial leads and fairly tall R waves over the left precordium. On the third hospital day there was a period of disorientation. A few basal pulmonary rales were still audible. The prothrombin content was less than 10 per cent. An electrocardiogram showed a normal sinus rhythm at a rate of 85; the PR and QRS intervals were 0.20 and 0.10 second, respectively; the ST segments were slightly sagging, and the T waves were diphasic in Leads 1, 2, aVF and V_4 through V_6; there were very deep S waves in the right precordial leads; the T waves were inverted, and the P waves were diphasic in Lead aVL. On the next day there was a steady substernal aching pain made worse with deep breathing. The neck veins were flat when the patient was raised 45°. The prothrombin content was 11 per cent. An electrocardiogram showed a normal rhythm at a rate of 85; the PR interval was 0.20 second; there was moderate sagging of the ST segments in Leads 1, 2 and aVL and considerable sagging in Leads V_4 through V_6; the precordial leads showed upright R waves from Lead V_2 through Lead V_6. By the fifth hospital day the pain had subsided. The white-cell count was 8400, and the sedimentation rate 51 mm. per hour. The prothrombin content was 16 per cent. For the next two days the prothrombin content was less than 10 per cent. The patient received 25 mg. of Dicumarol on the eighth hospital day when the prothrombin content was 18 per cent. On the tenth hospital day the white-cell count was

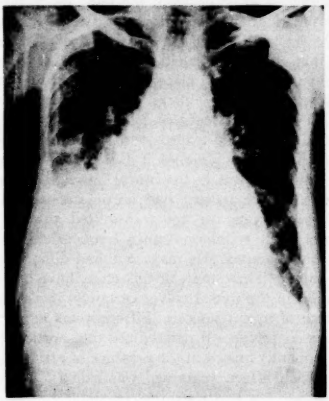

FIGURE 3. *Posteroanterior Film of the Chest, Showing Congestive Changes in Both Lungs, with an Abnormal Area of Density in the Right Base.*
The heart has further increased in size.

12,300, with 80 per cent neutrophils. The sedimentation rate was 49 mm. per hour. The total serum protein was 5.8 gm., the albumin 3.6 gm., and the globulin 2.2 gm. per 100 ml. The urine gave a + + test for albumin; the sediment contained 100 red cells and 200 white cells per high-power field; culture grew out moderate coliform bacilli. There continued to be episodes of atrial fibrillation with a rapid apical rate, and the loud friction rub remained the same in intensity. The prothrombin content gradually rose to 60 per cent. On the twelfth hospital day the patient suddenly felt nauseated, retched, became deeply cyanotic and apneic, and died.

DIFFERENTIAL DIAGNOSIS

DR. HOWARD B. SPRAGUE*: I am going to start this discussion by talking about the electrocardiograms — something that I deplore. The information distilled from them, I think, indicates that the patient showed left ventricular hypertrophy with additional digitalis effects, myocardial ischemia and probably some pericardial irritation (Fig. 2).

In a patient at the age of seventy who had no history of hypertension, a striking degree of left ventricular hypertrophy would most likely be the result of disease of the aortic valve. The story of a "leaky

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valve" for twenty-six years — a lay term that refers to a murmur due to obstruction or regurgitation — supports this supposition, as does the finding of a Grade 2 to 3 systolic murmur heard best in the aortic area and the fourth intercostal space and transmitted into the neck. The aortic second sound at one time was slightly less loud than the pulmonic and at other times seemed to be of about the same intensity. The patient had angina on effort for twenty-five years. Did he have disease of the mitral valve? There is a note that there was calcification in the area of the mitral valve. I always place this statement high in the category of what I might call evasive reporting on the part of the Department of Radiology. I should be happier if I could transport the calcium into the aortic valve than I should if I left it in the mitral valve, unless it was in the mitral annulus, because I believe that the patient had aortic stenosis. Apical systolic murmurs are not transmitted to the neck whereas aortic systolic murmurs frequently are transmitted to the apex. He may have had difficulty with both valves. There may, at this stage, have been calcification in the mitral valve; certainly, there was no evidence of mitral stenosis. Fifteen years ago at one of these conferences, I pointed out that aortic stenosis was frequently missed in the presence of atrial fibrillation, which fifteen years ago was called "auricular" fibrillation. He had the rapid irregular heart action of atrial fibrillation, with a drop in blood pressure; therefore, it was quite likely that the characteristic murmur of aortic stenosis would not be obvious. The blood pressure rose after the original episode, and normal rhythm was restored, but there was no further description of the murmur except when he was very ill. I conclude that the first attack of pain in the chest was caused by the occurrence of the rapid atrial fibrillation with the drop in blood pressure because rapid recovery with restoration of normal rhythm followed digitalization, and he was well for three months, except for slight angina. We do have to pay attention to urinary infections in these patients, who may insidiously acquire bacterial endocarditis on a diseased valve, but the later episode does not suggest a bacterial involvement of the valve to me.

May I see the x-ray films?

DR. RICHARD V. WILSON: I do not see the calcification of the mitral valve; I think that Dr. Joseph Hanelin thought that there might be a calcified valve and suggested that fluoroscopy be carried out. I assume that the calcification described is this intracardiac calcification. This is seen only in one film. Incidentally, some x-ray reports must be evasive, but when someone else tries to abstract those reports they are especially evasive. In the initial films taken during the first admission before the heart became greatly enlarged, there is fullness in the vicinity of the left ventricle and left atrium (Fig. 1). (This is an opinion without barium in the esophagus on a patient whom I did not examine at fluoroscopy.) The vessels in the lungs look somewhat prominent and are probably mildly congested. Four months later there is a great deal of congestion, and the heart is much larger (Fig. 3). There may be fluid in the pericardium although the angle that the right cardiac border makes with the diaphragm is against that. There is a great deal of fluid in the right pleural cavity. The shadows in the right-lung field may be due to the fluid, which may represent an infarct. There is a shadow here that also may be an infarction. The retrograde pyelogram does not contribute much. The left kidney is smaller than the right, but is not abnormally small.

DR. SPRAGUE: As far as the last incident was concerned, the diagnosis was already made for us because the patient received anticoagulants; therefore, it was believed that he had a myocardial infarction. I wish that I could be content with that diagnosis, but I am not, because the electrocardiogram is not diagnostic of the degree of myocardial infarction that clinically appeared to be present. Moreover, the blood pressure was well maintained, and the transaminase, although it was determined on the fourth day, was only 31 units.

I suppose that the rub was a pericardial rub; if that is so I believe I can rule out many of the causes of pericarditis, such as infections, uremia, a malignant process and acute idiopathic hemorrhagic pericarditis. It seems to me that there must have been an irritative substance, presumably blood, in the pericardium. The rub was not a striking two-way rub; there was more of a systolic element than a diastolic, but I should think it was pericardial rather than pleuropericardial or the result of friction between the pericardium and mediastinal structures. I do not believe there was evidence that this was due to seepage of blood into the pericardium from necrosis of the heart wall or that the patient had a ruptured heart. I am not going to reach into the bag to pick out a case similar to this that was discussed at one of these sessions, in which acute bacterial endocarditis was engrafted on aortic-valve disease, with rupture of a mycotic aneurysm of the coronary artery into the pericardium.[1]

I shall say that the sudden severe pain was most probably due to rupture of the aorta—that is, a dissecting aneurysm. There was not much to go with that; I shall have to stretch the data. There does not seem to have been evidence of dissection of the aorta distally, but I think that it had probably dissected toward the pericardium and coronary arteries. Apparently, the coats of the coronary arteries themselves are rarely involved in dissection because of their muscular character, but dissection around the coronary arteries may create pressure on them and may even result in secondary myocardial infarction. The friction rub was strikingly present on the second day, and I do not believe that is necessarily a differential diagnostic point between myocardial infarction and dissecting aneurysm. The drop in hemoglobin to 11.5 gm. per

100 ml. may or may not be significant. I do know of a case of silent rupture of an aneurysm into the abdomen in which a drop in hemoglobin was the key point to the fact that blood was leaking outside the circulation. The hallucinations, I think, could occur in anyone of this age who was as ill as the patient was so that I do not need to invoke obstruction of or pressure on the circulation to the brain.

What kind of aortic disease did he have? He had no history of rheumatic fever. He did have an aortic second sound, but there was no calcification in the aorta itself. Do you see any, Dr. Wilson?

DR. WILSON: No.

DR. SPRAGUE: If I concede that calcific aortic stenosis of the Mönckeberg type is a true entity, it has been pointed out in these conferences that it is often unaccompanied by atherosclerosis of the first portion of the aorta.

One type of aortic-valve disease that I shall suggest is a congenital bicuspid aortic valve, with secondary arteriosclerotic changes. It seems to me that this might be most consistent with the data, and it has been mentioned more than once in these conferences over the years. Maude Abbott[2] pointed out in 1927 that dissecting aneurysm of the aorta occurred with bicuspid aortic valves in a higher percentage of cases than would be expected on probability. There is no indication that the development of the systolic murmur at the apex was the result of more than dilatation; there was no suggestion of rupture of a chorda tendinea. I have an obsession that this man's trouble came from mischief in the region of the aortic valve. Since I have gone so far along this dogmatic road, I shall say that I think he had a congenital bicuspid aortic valve with secondary calcification, which is often association with other minor or major congenital anomalies; that there was a rupture of the posterior wall of the first portion of the aorta, with dissection along the coronary arteries and pericarditis; and that he died of a terminal massive dissection with bloody effusion in the pericardium. That is the way my logic works in this case, but as Lin Yutang once said, "A thing may sound so logical you are convinced it must be wrong."

DR. BENJAMIN CASTLEMAN: Did you mean that the pericardial rub was caused by hemorrhage resulting from the slow rupture of the aorta into the pericardium?

DR. SPRAGUE: I am not convinced that the first rupture necessarily was into the pericardium, but it may have been into the periaortic tissues or around the region of the pulmonary artery, with friction set up between the heart and those tissues. The final rupture was probably into the pericardium. The other possibility is slight leakage of blood at first with a rupture later. I do not know.

DR. KATHERINE E. SPRENG: When this patient was seen by Dr. Guillermo C. Sanchez in the afternoon of the day of the last admission there was no rub; one hour later, when I saw him, a very loud pericardial rub was audible over the entire precordium, with both systolic and diastolic components. Dr. Sanchez listened then and agreed that this was a new finding.

DR. CASTLEMAN: Dr. Barnum, you saw this patient; will you tell us your opinion?

DR. FRANCIS G. BARNUM, JR.: As Dr. Spreng has said, he was admitted for the last time by Dr. Sanchez, and I did not see him until the third hospital day. At that time it seemed to me that the problems were two: one was the therapeutic problem of controlling the paroxysmal atrial fibrillation, which was producing recurrent anginal attacks; the second was the diagnostic problem. On admission to the hospital the diagnosis was acute myocardial infarction, but with the absence of electrocardiographic changes and the persistence of the friction rub, we thought, as Dr. Sprague did, of dissection. We also seriously considered acute pericarditis and hemorrhage into the pericardial sac on an iatrogenic basis from the prolonged prothrombin time induced by Tromexan. Two additional urinalyses were not mentioned in the protocol, one showing 20 red cells and the other 100 cells per high-power field in the sediment.

About his death, at four o'clock in the afternoon, when he was seen by one of the house officers, the heart was fibrillating at a rate of 100; immediately before death one of the nurses found his pulse to be regular and of poor quality. It was our impression that he had had a pulmonary embolus. There was no statement about distention of the neck veins at the time of death. He was watched during the whole hospital stay for pulsus paradoxus, changes in blood pressure and distention of the neck veins as signs of cardiac tamponade, but none of these ever developed.

CLINICAL DIAGNOSES

Acute myocardial infarction, with mural thrombus.
Pulmonary embolus.

DR. HOWARD B. SPRAGUE'S DIAGNOSES

Rupture of first portion of aorta, with dissection along coronary arteries, hemopericardium and cardiac tamponade.
Aortic stenosis.
Congenital bicuspid aortic valve.

ANATOMICAL DIAGNOSES

Acute pericarditis, idiopathic.
Hydrohemopericardium (600 ml.), ?Dicumarol effect.
?Aortic stenosis.
Myocardial fibrosis, focal, left ventricle.
Calcification of annulus of mitral valve.

Pathological Discussion

Dr. Castleman: The pericardial sac contained about 600 ml. of hemorrhagic fluid — not pure blood; lining the pericardial cavity on the parietal layer was a great deal of fibrin. There was no rupture of the heart or of the aorta. There was, however, enough fluid in the pericardial cavity at the time of autopsy that it could well have acted as a tamponade. The aortic valve was somewhat thickened, but the cusps were not interadherent at their commissures. There was very slight calcification of the cusps. Beneath the aortic valve on the endocardium was fibrous tissue al-

Figure 4. *Heart, Showing Acute Fibrinous Pericarditis. Arrow points to endocardial fibrosis in the shape of an accessory cusp.*

most in the form of a cusp (Fig. 4). Ordinarily, when we see connective tissue being formed in this fashion, we think of aortic regurgitation. This fibrous tissue may have acted as an obstruction, especially since all the murmurs were systolic. The valve rings did not seem to be much narrower than normal. The heart was large, weighing over 600 gm., so that there must have been some degree of aortic stenosis. There was a calcification in the annulus of the mitral valve; I gather that that was what Dr. Hanelin saw in the films. The coronary vessels were normal; there was practically no arteriosclerosis.

How are we going to put all this together? I am not sure that I can. I think, as Dr. Barnum stated, that the effect of the Dicumarol aggravated a preexisting pericarditis which was the primary disease. How it arose, I do not know. The patient did not have uremic pericarditis; the kidneys were not diseased. We shall have to leave it as idiopathic pericarditis. Of course, he had evidence of heart failure; he had fluid in the chest. There were no infarcts in the lungs.

Dr. Myers saw this patient; he might like to comment.

Dr. Gordon S. Myers: When I saw him at the time of the first admission, I thought it likely that the discomfort in the chest was caused by coronary insufficiency precipitated by the onset of an arrhythmia. There was no definite evidence of a myocardial infarction. It seemed probable that he had coronary-artery disease with angina pectoris, in part because he had symptoms for such a long time. Patients with aortic stenosis, which we also believed he had, are not so likely to live for as many years after the onset of angina when that symptom is caused by the valvular disease. During the second admission I did not see him until about two days before death. At that time the friction rub had become very loud. Even though he did not have a rise in temperature, which we expect with hemorrhagic pericarditis complicating Dicumarol therapy, it seemed wise to stop the anticoagulant. Since the electrocardiograms had not shown diagnostic evidence of myocardial infarction it also occurred to me that there might be leakage of blood into the pericardium from a dissecting aneurysm. In all fairness, however, one must emphasize the fact that patients occasionally die of myocardial infarction without diagnostic changes in the electrocardiograms. I thought that myocardial infarction was a good possibility in this elderly man who had had angina for many years and had a sudden, severe episode of chest pain as described in the history.

This case raises a serious question. Should we give anticoagulants to patients who are suspected of having myocardial infarction if the diagnosis is doubtful? Certainly, with a leaking aneurysm or pericarditis, Dicumarol therapy cannot fail to be hazardous.

We might have learned more from this case if the heart had been perfused after death as Shaw and Goodale[3] have done in some of these cases. Anatomically, it was difficult to determine the degree of aortic stenosis, but clinically and logically, it seems that there must have been a significant degree of aortic stenosis. Even though a moderate amount of pericardial effusion was found, we cannot be sure that tamponade was present. Dr. Barnum was alert to this possibility and found no pulsus paradoxus or other evidence of tamponade before death.

Dr. Sprague: Accessory rows of aortic cusps have been found with or without bicuspid aortic valves and have been considered to be congenital anomalies by Maude Abbott[2] and others, when not the result of aortic regurgitation.* The other point that I wish

*Abbott says, in referring to "Anomalies of the semilunar cusps": "these cusps may be increased or diminished in number, and defective, fenestrated, or otherwise deformed. A row of supplementary cusps may exist or they may be the seat of attachment of anomalous bands." She mentions the occurrence of these cusps on the ventricular side of the aortic ring in association with aortic regurgitation from congenitally deformed valves but also in its absence.

to emphasize is that I know of 1 patient with acute hemorrhagic pericarditis who was suddenly stricken in the street with symptoms that suggested myocardial infarct; he had received no anticoagulants.

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CASE 42152

Presentation of Case

First admission. A sixty-six-year-old man entered the Emergency Ward because of abdominal pain.

For two weeks previously he had an upper respiratory infection. On the night of admission there was a sudden onset of persistent pain in the epigastrium. An hour later there was severe vomiting associated with chilly sensations.

He had been known to have diabetes for fourteen years and was taking 30 units of protamine zinc insulin; he had never followed a diet. There was a history of prostatic enlargement with nocturia for several years before entry.

Physical examination showed a well nourished man complaining of pain in the epigastrium. The left border of cardiac dullness extended 10 cm. to the left of the midsternal line. No murmurs were audible. Examination of the abdomen revealed severe tenderness in the epigastrium, with guarding and moderate spasm, greater on the right side. Peristalsis, which was absent, was noted on a later examination. No masses were felt. Rectal examination revealed marked prostatic enlargement.

The temperature was 102°F., the pulse 88, and the respirations 18. The blood pressure was 165 systolic, 80 diastolic.

The urine showed a trace of albumin with an orange test for glucose and a trace of diacetic acid; the sediment contained occasional white cells per high-power field. Examination of the blood revealed a hemoglobin of 14 gm. per 100 ml. and a white-cell count of 20,400, with 91 per cent neutrophils. The nonprotein nitrogen was 31 mg., the total protein 6.4 gm., the albumin 3.5 gm., the globulin 2.9 gm., the bilirubin 0.7 mg., and the fasting blood sugar 164 mg. per 100 ml. The alkaline phosphatase was 5 units. Cephalin flocculation was + + in forty-eight hours. The serum amylase was 179 and 256 units per 100 ml. (adapted from Somogyi — normal, 15 to 45 units). X-ray films of the chest and abdomen were normal except for slight elevation of the right leaf of the diaphragm and a somewhat tortuous and calcified aorta. An electrocardiogram showed nonspecific T-wave changes.

The white-cell count fell to normal on the day of admission. Treatment included gastric intubation, urinary-catheter drainage, fluids given intravenously, penicillin, streptomycin and insulin. The serum amylase fell to 37 units per 100 ml. on the first hospital day. The temperature gradually fell to normal. By the third hospital day there was no longer abdominal pain. The gastric tube was removed on the next day. On the ninth hospital day the serum amylase was 75 units per 100 ml., the cephalin flocculation was + + + in forty-eight hours, and the alkaline phosphatase was 11.7 units. A Graham test was unsatisfactory, and an upper gastrointestinal series was normal. After removal of the catheter there was acute urinary retention. Cystoscopic examination on the nineteenth hospital day revealed an enlarged median bar and a trabeculated bladder mucosa that appeared injected. The patient was discharged improved with an indwelling catheter on the twenty-sixth hospital day. The serum amylase was 75 units per 100 ml., and the alkaline phosphatase 5.1 units.

Second admission (two weeks later). A retropubic prostatectomy was performed, with removal of 60 gm. of prostatic tissue. Most of the enlargement was the result of a chronic granulomatous prostatitis, although there was also benign hypertrophy. The patient was discharged in good condition on the fourteenth postoperative day.

Third admission (two and a half years later). In the interval the diabetes was well controlled with insulin and diet. A urinary-tract infection was successfully treated with Gantrisin. About a year before admission an inguinal hernia on the right was noted. Physical examination showed an easily reducible indirect inguinal hernia on the right.

An inguinal herniorrhaphy was performed. On the fourth postoperative day there was a sudden onset of abdominal pain and tenderness in the right upper quadrant associated with nausea and vomiting of undigested food. The pain, which subsided with tincture of belladonna therapy, was similar in character to that noted during the first admission. On the next day there was a recurrence of the pain associated with vomiting. There was mild abdominal tenderness in the right upper quadrant. No spasm was noted, and no abdominal masses were palpable. Examination of the lungs was negative. The serum amylase was 16 Russell units (normal, 8 to 18 Russell units). After a slight response to tincture of belladonna the pain subsequently worsened. On the sixth postoperative day the temperature rose to 101.4°F. There was nausea, but no vomiting. The abdomen was moderately distended and tympanitic. There was some spasm in the right upper quadrant and splinting of the chest on the right. No abdominal rebound tenderness was present. Occasional peristaltic sounds were heard. There was bilateral calf tenderness that was greater on the left. The white-cell count was 21,200. The serum amylase was 8 Russell units. The cephalin

flocculation was ++ in forty-eight hours. X-ray films of the chest showed bilateral elevation of the diaphragm, linear atelectasis in both lung fields and some crowding of the lung markings. An electrocardiogram showed nonspecific T-wave changes. The temperature remained elevated. On the seventh postoperative day it rose suddenly to 103.3°F., with a chill two hours after an intravenous infusion, and subsequently fell to 101.6°F. The urine gave a + test for albumin and a green test for sugar; the sediment was normal. Examination of the blood revealed a white-cell count of 31,300, with 71 per cent neutrophils. The serum bilirubin was 1 mg. per 100 ml., and the amylase was 4 Russell units. The alkaline phosphatase was 3.9 units. A blood culture showed no growth. An intravenous pyelogram was normal. An electrocardiogram showed no significant changes.

On the next day an operation was performed.

Differential Diagnosis

Dr. James M. Shannon*: A sixty-six-year-old diabetic man entered the hospital for the first time with right-upper-quadrant and epigastric pain; he had an elevated temperature and white-cell count, and a diagnosis of pancreatitis was confirmed by an elevated blood amylase. He received routine therapy and recovered promptly. In the hospital x-ray films, including a Graham test and gastrointestinal series, were taken. I wonder if Dr. Hanelin would tell us what the radiologists mean by an unsatisfactory Graham test.

Dr. Joseph Hanelin: I assume that the radiologist thought there was a nonvisualized gall bladder. In the Graham series I am not certain that I can see any contrast substance in the gall bladder; if there is any, it is certainly faint. I do not see any opaque stones. The chest seems normal, and the abdominal films do not provide any clues to the nature of the trouble. The only real evidence of something wrong is the presumptive evidence of a nonfunctioning gall bladder. A gastrointestinal series done subsequently shows no intrinsic lesion, nor can I be certain of any widening of the duodenal loop, although there may be a pressure defect along the posterior aspect of the duodenum. Six months after the first admission — probably when he was an outpatient — a barium-enema examination was negative. I wonder whether in the postevacuation film we are visualizing a gall bladder without contrast medium within it that is perhaps slightly enlarged. The pyelogram done just before the last operation shows good renal function without displacement of the kidneys. There is some distention of the colon with gas.

Dr. Shannon: It is not surprising that urinary retention developed during the first admission. The second admission was for the purpose of having the prostate removed. Apparently, the patient had no trouble after that operation. The final admission is the one with which I am primarily concerned. I should like to ask whether he had any attacks of pain and discomfort in the interval of two and a half years between the second and final admissions.

Dr. Robert C. Coe: I do not recall; if he had attacks of pain, they were not severe enough to be contributory to the history.

Dr. Shannon: When the hernia was repaired, what was in the sac?

Dr. Coe: It was an inguinal hernia, with small-bowel in the sac.

Dr. Shannon: Was the cecum or appendix within the sac?

Dr. Coe: No.

Dr. Shannon: On the fifth postoperative day an acute inflammatory process developed in the abdomen. The first possibility is appendicitis. The appendix was not in the hernial sac, and the location of the pain and the course over the four days are certainly not typical of acute appendicitis. Another possibility, which Dr. Hanelin suggested by saying that the hepatic flexure was not well visualized, is acute diverticulitis. Acute diverticulitis of the right side of the colon is very rare, but it does occur and usually is mistaken for acute appendicitis. I think it, too, is unlikely because of the location of the pain and the fact that the patient had no evidence of diverticula in the x-ray films. A perforating duodenal ulcer causing pain and tenderness in the right upper quadrant should be considered, but the stomach and duodenum were normal and there were no symptoms referable to previous ulcer disease; therefore, I think I can rule that out, as I can renal disease by the normal intravenous pyelogram. Although diabetic patients are apt to have pyelonephritis, it does not seem to have been present in this case.

The one diagnosis that I think is probable is acute cholecystitis. The patient had had pancreatitis two and a half years previously, and there is certainly a well recognized correlation between biliary-tract disease and pancreatitis. That the cholecystogram was probably abnormal is further evidence of gall-bladder disease. The syndrome of acute cholecystitis after unrelated abdominal surgery is well known. Glenn and Wantz† recently discussed this problem and related it to the situation in which the patient after an operation becomes dehydrated and does not eat for two or three days; then, when he suddenly begins to eat, the inspissated bile and possibly stones in the gall bladder that were quiescent in the immediate postoperative period are suddenly forced through the cystic duct and may cause obstruction and acute cholecystitis. I think that that is the most likely diagnosis in this case. I do not think I can make the diagnosis of pancreatitis in the face of a normal blood amylase during the second admission.

*Clinical associate in surgery, Massachusetts General Hospital; surgeon, Salem Hospital.

†Glenn, F., and Wantz, G. E. Acute cholecystitis following surgical treatment of unrelated disease. *Surg., Gynec. & Obst.* **102**:145-153, 1956.

The patient's course was typical of a progressive, possibly gangrenous cholecystitis, with a persistently elevated temperature and a steadily rising white-cell count. I am sure that the surgeons caring for him hoped that they could put off an operation, but when the white-cell count rose to 31,000, the possibility of impending perforation forced their hands. I suspect that they did either a cholecystostomy or a cholecystectomy for acute cholecystitis.

DR. WINFIELD S. MORGAN: Dr. Coe, will you tell us the opinion on the ward?

DR. COE: The problem was one of high right-flank pain associated with known tenderness in the calf, a pre-existing urinary-tract infection and a nonfunctioning gall bladder, probably containing gallstones. When the patient first complained of the pain, it seemed to be pleuritic, and since there was calf tenderness we thought he had a pulmonary embolus. The films of the chest showed nothing to support that impression. The physical examination placed the process well out into the right flank; that fact confused us. The abdominal pain was not anterior or midclavicular, and there was no spasm anteriorly. Diseases of the urinary tract were considered, and we delayed another twelve hours while an intravenous pyelogram was done. Since that was normal, he was taken directly to the operating room with a preoperative diagnosis of acute cholecystitis.

CLINICAL DIAGNOSIS

Acute cholecystitis.

DR. JAMES M. SHANNON'S DIAGNOSIS

Acute cholecystitis.

ANATOMICAL DIAGNOSES

Acute cholecystitis, post-herniorrhaphy.
Cholelithiasis.

PATHOLOGICAL DISCUSSION

DR. MORGAN: A cholecystectomy was performed; the gall bladder as received in the laboratory was not abnormally dilated and measured about 3.5 cm. long. It was acutely inflamed, and the mucosa showed numerous superficial erosions. Microscopical sections revealed an acute inflammatory process superimposed on a chronic one with focal areas of gangrene. I think there was some question in our minds about whether this had perforated.

DR. COE: Dr. John D. Pitts, who performed the operation, found a poorly localized pericholecystic collection of pus.

DR. MORGAN: Postoperatively, what seemed to be signs of septicemia developed. The patient was extremely ill, and on the seventh day died suddenly from a massive pulmonary embolus. The pancreas did not appear abnormal at autopsy, and our microscopical sections did not give evidence of old pancreatitis. This suggests that the earlier attack of pancreatitis some two and a half years before death was a mild one.

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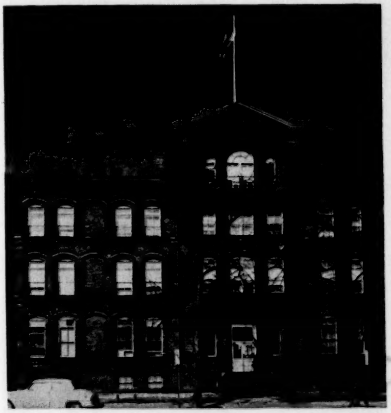
NATIONAL MEDICAL LIBRARY

THE action of Senators Lister Hill, of Alabama, and John F. Kennedy, of Massachusetts, in introducing on March 13 Senate Bill 3430 should meet with universal approval from the medical profession. The Bill, "to promote the progress of medicine and to advance the national health and welfare by creating a National Library of Medicine," was eloquently presented by Senator Hill, himself the son of a physician, and was ably supported by Senator Kennedy as cosponsor. Both authors were obviously well acquainted with the merits of their case, and under such expert guidance the proposed legislation should have excellent prospects for enactment.

The bill, as its introductory sentence implies, calls for the creation of an entirely new establishment, thus removing from the special jurisdiction of the Department of Defense what has been for years actually a medical library for the nation. According to the terms of the Bill the proposed library will be headed by a "Board of Regents . . . to be composed of the Surgeons General of the Army, Navy, Air Force, and Public Health Service, and the Librarian of Congress,



who shall be ex officio members, and twelve individuals appointed by the President by and with the advice and consent of the Senate and without regard to political affiliation."

Further important provisions of the proposed measure are that the Board shall appoint a director of the Library without regard to the civil service laws, that it shall have prepared drawings and specifications for the construction of a suitable building or buildings, that the usual functions of a library shall be performed and that, "at the earliest practicable moment," the President shall "provide for turning over to the National Library of Medicine the existing Armed Forces Medical Library, its collections, records and equipment."

The present paradoxical situation whereby what is considered the largest and most important medical library in the world happens to be a responsibility of the armed forces of the United States is a matter of history continuing to develop in the channels where it originally started. The Library was founded in 1836, more or less casually, as the Library of the Surgeon-General's Office, United States Army. As Senator Hill noted, in the speech with which he introduced the Bill, it achieved greatness during the thirty-year librarianship of Colonel John Shaw Billings, which began in 1865. It was during this period, in 1887, that the Library was installed in the building, now superannuated, where it is still mainly housed, although since 1942, for lack of space in Washington, a large part of its material has been deposited in rented facilities in Cleveland, Ohio.

The Library at present contains nearly a million books in addition to outstanding collections of theses, portraits and photographs and documents of various importance. Some 100,000 journals and monographs are received yearly, including over 10,000 periodical publications, much of this material being inadequately protected from the weather and subjected to an unavoidable neglect under present conditions, which if continued could, as Senator Hill pointed out, rob the nation and the world of this treasure. Moreover, it would be absurd, as has also been indicated, for a Department of Defense, occupied with grave matters of an entirely different nature, to concern itself with an almost academic project so foreign to its usual duties.

A national medical library to be administered by a board responsible only to Congress has been proposed after studies and deliberations that have extended over a number of years. The Task Force on Federal Medical Services of the Hoover Commission has recommended it. The surgeons general favor it, as does Colonel Rogers, the present librarian and the logical choice to occupy the larger post with the proposed institution, and a carefully conceived bill has been introduced to make it a reality. At this juncture the enlightened and enthusiastic support of the nation's physicians should also be thrown into the balance.

CONFERENCE ON CHEMOTHERAPY OF TUBERCULOSIS

THE fifteenth Veterans Administration-Army-Navy Conference on the Chemotherapy of Tuberculosis recently held in St. Louis marked the end of a decade of a highly successful program designed to evaluate the antimicrobial therapy of tuberculosis and to put the results to use in a manner that would bring the greatest benefit to patients afflicted with the various forms of this disease. The great interest in the activities of these conferences is evidenced by the increasing attendance, which this year surpassed 400 registrants from this country, with some from Australia, Canada and France.

Carefully controlled data from some 3300 patients with pulmonary tuberculosis has reaffirmed the conclusion, previously reached from earlier data, that in patients with well advanced disease isoniazid combined with para-aminosalicylic acid gave the most satisfactory results of any combination of agents tested. A random comparison of triple drug therapy (that is, these two in addition to streptomycin) did not show any superiority over the regimens employing only two drugs. Judgment was still reserved, however, for patients having very large cavities, since too few such cases were observed. No conclusion was reached on the optimum duration of therapy beyond the general agreement that prolonged chemotherapy is superior to short-term treatment.

Further reports on the combination of isoniazid and pyrazinamide again confirmed the high degree of effectiveness of this therapy. Hepatotoxicity was still being observed but did not seem to be quite so frequent or so serious as was suggested from some of the reports presented at the Conference last year.

A report was also given on the results of a random study of cycloserine, the agent that was first presented to the Conference in 1955. A total of 204 patients were observed, 93 of them having received 1.0 gm. of cycloserine daily, whereas 111 were treated with the usual regimen of isoniazid and para-aminosalicylic acid. Moderate to marked improvement on x-ray study and conversion to negative cultures were observed significantly less often in patients receiving cycloserine alone than in those receiving the combination of isoniazid and para-aminosalicylic acid. Failure to improve clinically and actual relapses were more frequent among the patients receiving cycloserine. Preliminary observations on the use of cycloserine in combination with isoniazid suggested that the therapeutic effect was enhanced. The major toxic effect from cycloserine was the occurrence of convulsions, but according to some of the participants, these could apparently be reduced or perhaps even abolished by a reduction of the dose.

A preliminary report was presented by workers at Fitzsimons Army Hospital on the effects of free ambulation during the course of chemotherapy. It was tentatively concluded that hospitalized patients permitted to ambulate freely fared no worse than those restricted to a modified bed rest.

One of the highlights of the Conference was the showing of a film entitled "Dynamics of the Tubercle," which was prepared by Drs. R. H. Ebert and W. R. Barclay, of the University of Chicago. This contained an animated visual analysis of the specially prepared chamber in the rabbit's ear in which the development of the tubercle could be observed both in the primary infection and in the reinfection type of lesion. What was most impressive, however, was the direct observation of the effects of the antimi-

crobial agents that could be clearly visualized in these preparations.

A number of important pilot studies were planned to answer various other questions among those raised during the course of this conference and in the meetings of its committees. These may be expected to yield an additional crop of useful and practical answers, some of which may be available at the time of the next conference.

CHARITY AND EDUCATION

THE establishment of a charitable and educational fund within the Massachusetts Medical Society was first proposed to the Council by the Committee on Finance at the meeting of February, 1955. The Society at that time was unable to avail itself of a potential gift or legacy because of the prospective donor's liability to gift or inheritance taxation. Such a gift or bequest, however, could properly be received into a special fund, independent of the usual administrative facilities of the Society and established for the sole purpose of promoting its laudable designs.

The measure as proposed by the Committee on Finance did not meet the approval of the Council and was referred back to committee, its acceptance being delayed until the following October. The provisions under which the fund was finally instituted and will operate are given in detail elsewhere in this issue of the *Journal*.

The Charitable and Educational Fund forms in a way a triad with the Massachusetts Medical Benevolent Society and the Committee on Benevolence of the Massachusetts Medical Society, and should not be confused with either of these charitable establishments. The Benevolent Society, about to celebrate its hundredth anniversary, is no part of the Massachusetts Medical Society, although linked to it by the closest ties of mutual humanitarian endeavor; the Society's Committee on Benevolence, authorized in 1948 to help care for needy members of the profession and their families, functions largely through the allocation to the Benevolent Society of funds appropriated by the Council for the purpose. These two have indispensable but narrowly specific objectives.

The new fund, subject to its unpredictable future growth, has actually been brought into concrete being by an appropriation of $5,000, which amounts to a practical sharing of the customary appropriation for the needs of the Committee on Benevolence; it may serve a variety of purposes within its legal dimensions. Already, scholarships have been proposed, aid to the Postgraduate Medical Institute and assistance as yet unspecified in the education both of the profession and the public.

Another suggested service that it might adopt, which would not tend to disperse either principal or income, would be the setting up of a revolving loan for qualified medical students and interns. No doubt other uses will be devised, their scope depending on the growth of the Fund itself.

ALOHA

THE medical profession of the Mainland, even so far away as the Atlantic seaboard, sends greetings to the Hawaii Medical Association on the occasion of its centennial celebration and scientific congress, to be held from April 22 to April 29. It is not necessary to accompany these good wishes with flowers, even in a figurative sense, for Hawaii is itself the land that perennially blossoms.

The history of the Association is told in the April issue of the *Hawaii Medical Journal* by its editor, Dr. Harry L. Arnold, Jr. According to this highly informative document the Privy Council of the Kingdom was called together on May 19, 1856, for two purposes — to announce the impending marriage of young King Kamehameha IV to Emma, daughter of Dr. T. C. B. Rooke, of Honolulu, and to consider a petition of 10 physicians of the city, including Dr. Rooke, for a charter of incorporation as a medical society. In this manner and at this time the Hawaiian Medical Society came into being.

Except for a rare newspaper account of a meeting, however, the Society, like Alph, the Sacred River, apparently then went underground for a number of years. In 1890, urged on by Dr. John S. McGrew, the doctors of Honolulu reorganized and in 1895 adopted the Constitution and By-Laws of the "Medical Association of Hawaii." One of the requirements for membership was graduation from a medical school recognized by the American Medical Association, although Hawaii was still an independent monarchy, not to be annexed to the United States until the following year. Records appear still to have been considered unnecessary since the first ones that can be found were for the meeting of January 3, 1913.

Patriotically active in World War I, the members of the Association seem also to have been a politically conscious group; in 1924 a bill of $70 for Christmas cigars for traffic policemen was approved without question.

In the following year county societies were established, and the name Hawaii Territorial Medical Association was adopted for the parent body as distinct from the Honolulu County Medical Society, Honolulu County comprising the Island of Oahu. Three years later, in 1928, rotation of meetings among the major islands began, but it was not until 1941 that the title "Hawaiian Medical Society" was legally changed to "Hawaiian Territorial Medical Association" on the basis of the original still-valid charter of 1856. In eighty-five years the wheel had turned a full cycle and the Association had come back to its beginnings.

At the same time the Association's *Transactions*, which had been published as such since 1900 and

had become a monthly bulletin in 1938 reached full status as the *Hawaii Medical Journal*. Since 1944 the *Journal* has been under the management of Mrs. Edith C. Bennett, who in that year became executive secretary of the Association and who, with her group of native minstrels entertained and charmed the clinical session of the American Medical Association in Boston last fall.

As a final item of historical interest the Association, anticipating statehood for the Islands, dropped "Territorial" from its name in 1953. Certainly when statehood is achieved the archipelago, unique for the friendliness of its internal relations, will be warmly welcomed by the rest of the country.

Providence Medical Association. — *We have received a copy of the by-laws of the above association, relating to fees and to professional etiquette. The fee for a regular visit is the same as that in Boston.*

Boston M. & S. J., *April 17, 1856*

MASSACHUSETTS MEDICAL SOCIETY

CHARITABLE AND EDUCATIONAL FUND

At the October, 1955, meeting of the Council a charitable and educational fund was established with the following provisions:

1. The principal of the Fund shall never be used for any purpose other than charitable and educational ones.
2. The income from the Fund, when not added to the principal, shall be used exclusively for such purposes.
3. The Fund is to be administered by a board of directors, five in number, all members of the Massachusetts Medical Society, appointed by the president, and approved by the Council, for terms of one, two, three, four and five years initially and thereafter one each year, this board to have specific control over investments made by the Treasurer, subject to the approval of the Committee on Finance, and to have specific control, subject to the approval of the Council, over:

   a) The acceptance of bequests and legacies in the name of the Massachusetts Medical Society, made to the Fund as such, and
   b) The specific distribution of income for charitable and educational contributions, no part ever inuring to the benefit of any private individual, and no part to be used for propaganda, or influencing legislation or promoting a political campaign, with such distributions being made by the treasurer drawing on the Fund's special account, only as authorized by the board of directors and approved by the Committee on Finance of the Massachusetts Medical Society.

4. Should the board ever recommend dissolving the Fund with distribution of the principal for exclusively charitable and educational purposes, this action is to be taken only after approval by the Council.
5. All benefits during the tenure of the Fund or its dissolution are to be confined to Massachusetts or a state or combination of states with which Massachusetts has reciprocity on these matters.

This outline has been submitted to the Department of Internal Revenue, Washington, and the Massachusetts State Department of Taxation, neither of which expresses objection. The last paragraph was inserted at the suggestion of the legal bureau of the Massachusetts Department of Taxation to cover a bill, Senate 524, which is to be introduced very soon and which is expected to be passed without opposition. Twenty-three states have such reciprocity with Massachusetts, and 16 more have no inheritance tax at all. The Committee on Finance recommends the establishment of such a fund as set forth above.

At the meeting of the Council on February 1, 1956, Dr. Wesselhoeft proposed the names of the following directors: Dr. Hyman Morrison, Dr. Walter Phippen, Dr. Nicholas Scarcello, Dr. Charles G. Shedd and Dr. Charles C. Lund, *chairman*. They were elected by the Council.

The directors held their first meeting on February 29, 1956. All the directors and Dr. Eliot Hubbard, Jr., treasurer of the Society, were present. At this meeting Dr. Hubbard announced that $5,000 was already available that had been donated to the Fund by the Society at the February Council meeting. The directors proceeded to authorize Dr. Hubbard to invest most of this money already approved by the Committee on Finance, about half in stock of Standard Oil Company of California and the other half by deposit in the Provident Institution for Savings in Boston. A small amount is to be left in the checking account.

It was further voted that for the present all income received by the Fund shall be added to the capital.

The directors then discussed ways and means of making this fund effective. It was agreed that the most important immediate effort should be to inform the fellows of the Society of the existence of the Fund and obtain their co-operation in determining the best uses for it.

Two possibilities that already appeal to one or more members of the Committee are efforts toward education of the public in the facts of medicine and education of doctors concerning important developments in medicine.

Suggestions concerning the Fund will be gratefully received by the Committee and should be sent to the chairman of the directors at the office of the Society, 22 Fenway, Boston.

CHARLES C. LUND, M.D.
Chairman

TREASURER'S REPORT COVERING DISTRICT DISTRIBUTION

The Committee on Finance has voted to distribute the sum of $6,000 for the year 1956 to the district societies toward defraying their operating expenses.

The total number of payments received by March 1, in time to count for the distribution, was 4868 — an increase of 150 over 1955. The amount for each paid member comes to $1.2325.

The following table gives the number of payments as of March 1 for each district. The actual amount of the distribution to each district is shown as of March 22, 1956.

District	No. Reported Paid	Amount Distributed
Barnstable	64	$ 78.89
Berkshire	127	156.54
Bristol North	73	89.98
Bristol South	190	234.19
Charles River	468	576.82
Essex North	175	215.70
Essex South	279	343.88
Franklin	45	55.47
Hampden	357	440.01
Hampshire	66	81.36
Middlesex East	133	163.93
Middlesex North	109	134.35
Middlesex South	569	701.30
Middlesex West	123	151.61
Norfolk	747	920.68
Norfolk South	163	200.91
Plymouth	132	162.70
Suffolk	612	754.29
Worcester	340	419.06
Worcester North	96	118.33
	4,868	$6,000.00

Eliot Hubbard, Jr., M.D.
Treasurer

CORRESPONDENCE

TREATMENT OF DISK HERNIATION

To the Editor: The article by Dr. Donald Munro, "Lumbar and Sacral Compression Radiculitis," in the February 9 issue of the *Journal*, deals with an important clinical problem: low-back and sciatic pain of intervertebral-disk origin. Several aspects of his interesting paper call for critical comment.

He describes a radical operative technic for dealing with disk herniations that he considers superior to those in common use. The technic that he advocates includes routine transdural exploration and incision of the tight root sheath. Is it not likely that the "tight dural sheath" that he advocates treating by incision is only relatively tight around an edematous nerve root and that the tightness will disappear when the edema of the decompressed nerve root subsides? The incidence of serious postoperative complications that he reports (17 cases of bladder paralysis in 375 operations) is distressingly high. An extradural exposure and removal of the disk lesion would seem less likely to damage the roots of the cauda equina.

Dr. Munro advocates an extensive laminectomy in order to expose the lesion. Although we can agree that too little operative exposure is harmful, his statement that "too much exposure is harmless" calls for validation. Unfortunately, operative exposure in disk surgery necessitates sacrifice of a certain amount of functioning skeletal tissue, but excessive removal of bone, elastic ligaments and apophyseal joints is *not* always harmless, and on the contrary is likely to increase the incidence and severity of postoperative weakness and pain in the lower back.

It is interesting that Dr. Munro limits his patient to work "that does not require lifting, jumping, pulling or pushing, or working with his back in a strained, unnatural position for even relatively short periods. These limitations will apply for the rest of his life at work and at home." Is imposition of these severe limitations on physical activity a tacit acknowledgment of failure of this method of treatment to provide a back strong enough to stand up to ordinary daily physical activity? Among the numerous reports on the operative treatment of disk lesions, the classification of excellent or good has been reserved for patients who are found at end-result study to be free of pain and to have a back that functions well under the ordinary stresses of daily physical activity. The restriction that Dr. Munro places upon his patients would make it impossible for the end-result rating (as yet unpublished) of any of his cases to be classified as better than fair.

He dismisses the combined excision-fusion operation as absolutely contraindicated, and yet his experience with this operation is by his own statement limited to 3 cases. Previously published end-result studies give ample evidence that simple disk excision (by radical or limited exposure) leaves at least 50 per cent of the patients so treated with some back symptoms. In an attempt to improve these results, a considerable number of skilled surgeons are adding a local fusion operation to the procedure of disk excision, and several carefully documented end-result studies indicate that the combined operation is superior to disk excision alone. It is to be hoped that Dr. Munro's enthusiastic endorsement of extensive exposure by transdural approach and his denunciation of the fusion operation will be received *cum grano salis*. His efforts to improve operative results deserve commendation, for the back problem is still far from solution.

Joseph S. Barr, M.D.

Boston, Massachusetts

MOUNT AUBURN HOSPITAL CONTROVERSY: ANOTHER VIEW

To the Editor: Recently, a great deal of discussion about the affairs of the Mount Auburn Hospital has been directed to you by Dr. Charles H. Bradford. He believes that important principles of consequence to the Mount Auburn and other hospitals are involved.

The undersigned members of the staff do not agree with the views expressed in the letters of Dr. Bradford but prefer to refrain from further public utterances, at present, since the matter is now in the hands of the Committee on Hospital and Professional Relations of the Massachusetts Medical Society. We believe that such publicity tends to prejudge the case. We prefer to allow this committee to collect the facts on an impartial basis.

Meanwhile, we find nothing in the new bylaws that prevents any member of the staff from practicing in the highest traditions of the medical profession.

Thomas W. Botsford
Madelaine R. Brown
Bradford Cannon
Leo J. Cass
Chilton Crane
Neil L. Crone
Edward J. Durling
R. Cannon Eley
John E. Gary
Dwight E. Harken
William R. Hill
David Hurwitz
Wyland F. Leadbetter
Samuel Lowis
H. Edward MacMahon
William C. McCarty
Paul H. Means
Dudley Merrill
Robert H. Morris
Gordon A. Saunders
Albert O. Seeler
Richard Schatzki
Joseph Tartakoff

THERAPEUTIC MIRAGES?

To the Editor: I read with interest Dr. Grace A. Goldsmith's Medical Progress report, "Current Status of the Clinical Use of Antibiotic-Vitamin Combinations," in the January 26 issue of the *Journal* and also the editorial, both of which seemed to me to deal too gently with a hazard on the therapeutic horizon that may be nothing more than an example of the enormous variety of untested therapeutic regimens being thrown at the heads of physician and patient alike. It seems to me to be stretching the point of gullibility to believe that manufacturers of vitamins and pharmaceuticals are obliged to take as mandate the admittedly rather loose implications of the report on "Therapeutic Nutrition."

One is forced to admit, however, that the mandates, real or imaginary, are never taken when they reduce business of the pharmaceutical manufacturers, but only when they add, or potentially add, to their sales. It seems quite improbable that vitamin manufacturers will have on their staffs enough scientists and skeptics to counterbalance those in charge of promotions and sales; in fact, such people generally have little voice in the policies of the larger companies. Pending such developments, it is necessary for medical journals, as well as individual investigators, to keep the most scrupulous standards of demonstration and objectivity before accepting the complete equivalence of "stress" and "infection." I have expressed elsewhere the view that responsibility for introducing new combinations of drugs lies with both the manufacturers and the physicians. Now that the American Medical Association no longer has even a nominal testing agency, it may be necessary to form some collaborative testing facility employing teaching hospitals as a likely place and having the financial as well as judicial monitoring of the pharmaceutical industry.

WILLIAM B. BEAN, M.D.
Professor of Medicine
State University of Iowa College of Medicine
Iowa City, Iowa

OF SLIPS AND SALE AND WAXING SERENDIPITEOUS

To the Editor: In answer to Llewellyn Sale on page 293 of the February 9 issue of the *Journal,* I submit the following:

A Missouri physician named Sale
Is "startled, but pleased" to bewail
Pleonasms of others
(His medical brothers)
Which he finds now and then in his mail.

For me, the supreme serendipity
Creating less heat than humipity
When accorded the time
Is to dabble in rhyme
Which I usually call pervers(ip)ity.

ELLIOTT S. ROBINSON, JR., M.D.
Lewistown, Pennsylvania

TEXTBOOKS AND JOURNALS WANTED

To the Editor: I wish to inform you that St. George's Mission Hospital is a nonprofit organization situated in a hilly village and working among the poor, laboring classes of Punalur and its suburbs. Since good medical literature is very scarce in this part of the world, a small library was recently started attached to the Hospital with the idea of collecting used medical journals, books, bulletins, reprints of articles and transactions of medical societies from all available sources in foreign countries so that up-to-date knowledge in medical practice could be obtained.

Furthermore, Ayurvedic and Unani systems of medicine are very troublesome competitors to the Allopathic system here, and proper equipment and medical literature are highly essential for the successful management of the Hospital. We should accordingly be grateful for used medical journals, with all available back copies, medical books, reprints of articles and other useful medical literature, as well as any second-hand surgical instruments, medical appliances and laboratory equipment that can be spared. Many of our poor patients may directly and indirectly be benefited by them.

T. K. THOMAS
Hon. Medical Superintendent
St. George's Mission Hospital
Punalur
Tranvancore, South India

PROGESTERONE IN PSYCHIATRY

To the Editor: In the article, "Use of Progesterone in the Treatment of Post-Partum Psychosis," in the January 26 issue of the *Journal,* Drs. Bower and Altschule come to conclusions that cannot be supported by the data presented. A rudimentary acquaintance with statistics (such as mine is) makes it apparent that there is no statistical basis for the inference that progesterone is therapeutically valuable in the treatment of post-partum psychosis.

A colleague skilled in statistical technics reviewed this paper at my request. By the method of the significance of the difference of proportions, an "x" value of 0.68 is found; this value will occur by chance in comparisons of samples of this size in at least 25 per cent of cases. The final sentence of this article says, "The use of progesterone increased the remission rate in post-partum psychosis to almost 100 per cent." This consultant's comment is: "'Increased' is not defensible, since the rate without progesterone is 87 per cent, and the rate with it is only 94 per cent, not a statistically stable shift."

From an examination of the data, it is easy to draw a conclusion that the remission rate in the whole group approximates 90 per cent, no matter what method of treatment was used.

It seems important to call this matter to your attention because the estimation of the efficacy of therapeutic agents in psychiatric conditions is difficult enough at best, and it behooves investigators in this field to utilize the tools (primarily statistical ones) available for accurate determination wherever applicable.

HARLEY C. SHANDS, M.D.
Associate Professor of Psychiatry
University of North Carolina
Chapel Hill, North Carolina

Dr. Shands's letter was submitted to the authors of the paper in question, who offer the following reply:

To the Editor: It is not quite clear what Dr. Shands and his skilled colleague are trying to prove or disprove. It was not the purpose of our article to show a statistically significant difference in ultimate outcome between patients treated with and those treated without progesterone; it is obvious that the follow-up period was much too short for that. It was our thesis that although the initial remission rates were about the same, the relapse rate was 50 per cent without and 6 per cent with progesterone. The incidence of lasting remission without relapse was significantly different in the two groups.

In addition, the observation that in several cases (particularly Cases 3, 7 and 8) results without progesterone were discouraging because of repeated relapses, whereas rapid and lasting improvement occurred with progesterone, is significant, since each case was its own control.

It is generally agreed that estimation of the efficacy of therapeutic agents in psychiatric conditions is difficult.

WILLIS H. BOWER, M.D.
MARK D. ALTSCHULE, M.D.
Waverley, Massachusetts

BOOK REVIEWS

Hearing Therapy for Children. By Alice Streng, M.A., LeRoy D. Hedgecock, Ph.D., James W. Phillips, M.D., Waring J. Fitch, M.A., and James A. Carrell, Ph.D. 8°, cloth, 371 pp., with illustrations and tables. New York: Grune and Stratton, Incorporated, 1955. $6.75.

This book, written not only for the trained otologist, who makes the diagnosis, the audiologist, who tests the extent of the disability, and the teacher but also, mainly, for the parents of deaf children, answers their questions about what can be done and how such children can be trained to find a place in the community. It is well written, with an excellent presentation of the problems of the deaf child. It explains and demonstrates with charts and lessons what can be done and what must be done for the child who has lost the sense of hearing.

The book consists of eight main chapters, with an appendix and a good index. The introductory chapter gives the history of the progress made in the teaching and rehabilitation of the deaf child. The problems are then discussed in a clear and understanding manner.

The second chapter, which analyzes both the acquired causes secondary to disease and the inherited types, is written so that a layman can understand it without difficulty. There are several errors that should be corrected in future editions, which the book undoubtedly will have. On Page 23 the illustration represents the high tones being heard on the broadest part of the basilar membrane with the low tones at the narrowest part. This should be reversed. The statement on Page 37 that partial stenosis of the external auditory canal causes loss of hearing is not true and should be corrected. In discussion of otosclerosis on Page 46 the statement is made that in otosclerosis, air conduction is 30 decibels or more above (or worse than) bone conduction. This is a reversal of the base line (0 line) used in the audiometric charts presented in later chapters and may cause some confusion to the lay readers.

The next 2 chapters, audiometry and clinical audiometry, can also be understood by any nontechnical person. The chapter on the use of hearing aids for children is not only important but also extremely well presented. The emphasis of introducing the child to sound effects before the hearing aid is used is well taken and significant. The general criteria for their use as early as possible are well presented.

In the remaining chapters, devoted to training of the child, there are three groupings of the patients: the mildly and the severely afflicted and the profoundly deaf, a chapter being given to each. Methods of training are discussed; there are numerous charts, and actual lessons are given, with full instructions in their use. These chapters are most valuable to the parents, for they give hope that a great deal can be done for the child. The discussion of schooling is taken up, but no mention is made of the desirability of integrating the deafened child with normal children in school. If the handicap can be overcome by a hearing aid, auditory training and lip reading, the deaf child should be with normal children at all times and not in a special school.

At the end of each chapter there is an excellent bibliography and, what is more important in many ways, an appendix listing all the established rehabilitation centers of the country.

This book is a must for the parents of a deafened child and can be read with a great deal of benefit by the otologist, the audiologist and the teachers of the deaf. It gives a stimulating and excellent presentation of the problems of the deafened child.

MOSES H. LURIE, M.D.

Differential Diagnosis: The interpretation of clinical evidence. By A. McGehee Harvey, M.D., and James Bordley, III, M.D. 8°, cloth, 665 pp. Philadelphia: W. B. Saunders Company, 1955. $11.00.

The clinicopathological case discussion has become firmly established in American medical centers over the decades since its inception at the Massachusetts General Hospital. The authors of this book are to be congratulated on the success with which they have applied this method of teaching to some of the aspects of differential diagnosis. They have accomplished this by grouping cases selected from those presented at the clinicopathological conferences at the Johns Hopkins Medical School.

The careful collection of facts followed by the systematic analysis of those facts will lead, in the majority of cases, to a correct diagnosis. This thesis is repeatedly stressed in the numerous examples of successful analyses contained in the book. Some 30 tables help to group etiologic considerations.

Each chapter dealing with some important symptom, sign or group of diseases is introduced by a discussion of the causes of the condition under study, and this is followed by several clinicopathological case analyses illustrating the general subject. Of particular interest are the chapter, "Special Diagnostic Problems Including the Diagnosis of Certain Rare Diseases," with 27 illustrative cases, and a section of 11 unknown cases with discussion and solutions in later pages.

The authors are well aware of the limitations of this type of presentation, focusing as it does on fatal cases and emphasizing the more difficult diagnoses, but the advantages of using actual patient problems as they confront the physician are considerable and more than compensate for any disadvantage. No attempt is made to compete with the more encyclopedic type of reference work on differential diagnosis. The stress is on intelligent analysis and the reasoning aspects of diagnostic acumen rather than the presentation of long lists of diseases that have been known to give rise to a given symptom.

In the reviewer's opinion, the use of a few well placed roentgenographic reproductions would improve the case presentations and more than compensate for the slight increase in size that their inclusion would entail. This is particularly true in the chapter entitled "Diseases Involving the Lungs or Mediastinum."

Although this book should be of great interest to all practicing physicians and medical students, it is perhaps of greatest value to the thousands of physicians who do not reside in areas where this type of postgraduate teaching is available. It is to be hoped that this excellent work will stimulate others to undertake similar projects, for the subject is far from exhausted.

JOHN W. NORCROSS, M.D.

Bronchus und Tuberkulose: Bronchoskopische und bronchographische Untersuchungen der Bronchen bei der Tuberkulose. By Dr. Med. A. Huzly and Dr. Med. F. Böhm. 4°, cloth, 138 pp., with 258 illustrations. Stuttgart: Georg Thieme, 1955. DM 57.- $13.55. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

This is an excellent monograph on bronchial changes accompanying tuberculosis. The book is profusely illustrated with copies of roentgenograms and diagrams, some of which are in color.

One has the impression that a great deal of time and effort has been spent to present the findings based upon the detailed observation of 1500 patients over a number of years. The various chapters deal with bronchial changes encountered in parenchymal tuberculosis; the problem and significance of bronchial perforation by tuberculous lymph nodes; bronchial deformity produced by changes that follow pleurisy; and tuberculosis of the bronchial walls. The last portion is extremely well documented by illustrations of bronchoscopic findings (in color), pathological specimens, diagrams and an abundant selection of excellent bronchograms. The incidence of acute endobronchial tuberculosis is estimated as being about 10 per cent of examined cases. At the present time, with appropriate antituberculous drug therapy, the problem of tuberculous endobronchitis is becoming one of decreasing significance, but the entity remains, however small.

An extensive list of references is given, and the experience found in the literature has been used in the discussion together with the author's observations.

This monograph does not represent any new progress, but does present a comprehensive picture of the over-all problem. The chief detraction from its value is that the printing is in German; although it may serve as a reference book, it probably will not be read by too many of those concerned with this specific problem.

RICHARD H. OVERHOLT, M.D.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Atopic Dermatitis. Edited by Rudolf L. Baer, M.D., associate professor of clinical dermatology and syphilology, New York University Post-Graduate Medical School. 12°, cloth, 112 pp., with 6 illustrations and 3 tables. New York: New York University Press: 1955. $2.50. (Distributed by J. B. Lippincott Company, Philadelphia.)

District Nursing: A handbook for district nurses and for all concerned in the administration of a district nursing service. By Eleanor Jeanette Merry, S.R.N., S.C.M., M.C.S.P., Q.N. & H.V.Certs., social studies cert., Bedford College, general superintendent, Queen's Institute of District Nursing; and Iris Dundas Irven, S.R.N., S.C.M., Q.N. & H.V.Certs. Second edition. 8°, cloth, 262 pp., with 15 illustrations and 9 plates with frontispiece. London: Baillière, Tindall and Cox, 1955. $4.50. (Distributed by Williams and Wilkins, Baltimore.)

How to Reduce Surely and Safely. By Herbert Pollack, M.D.,; with Arthur D. Morse. 8°, cloth, 157 pp., with illustrations and tables. New York: McGraw-Hill Book Company, Incorporated, 1955. $2.95.

Classics of Biology. By August Pi Suñer. With an authorized English translation by Charles M. Stern. 8°, cloth, 337 pp. New York: Philosophical Library, 1955. $7.50.

Die Überfunktion der Nebennieren. By Rudolf Chwalla. 8°, cloth, 330 pp., with 12 tables. Vienna: Wilhelm Maudrich, 1955. $12.00. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

Polio Pioneers: The story of the fight against polio. By Dorothy and Philip Sterling. 8°, cloth, 128 pp., with photographs by Myron Ehrenberg and the National Foundation for Infantile Paralysis. New York: Doubleday and Company, 1955. $2.75.

Public Health: Its promise for the future: A chronicle of the development of public health in the United States, 1607-1914. By Wilson G. Smillie, M.D., D.P.H., professor of public health and preventive medicine, Cornell University Medical College. 8°, cloth, 501 pp., with 50 illustrations and 19 tables. New York: The Macmillan Company, 1955. $7.00.

Klinische Elektrokardiographie. By Dr. Max Holzmann, Zurich. Third edition. 8°, cloth, 688 pp., with 303 illustrations and 4 tables. Stuttgart: Georg Thieme, 1955. DM 80.- $19.05. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

Administrative Medicine: Transactions of the Third Conference, October 6, 7, and 8, 1954, Princeton, New Jersey. Edited by George S. Stevenson, M.D., national and international consultant, National Association for Mental Health, New York City. 8°, cloth, 172 pp. New York: Josiah Macy, Jr., Foundation, 1955. $3.00.

The Psychoanalytic Study of the Child. Vol. 10. Edited by Ruth S. Eissler, M.D., et al. 8°, cloth, 400 pp. New York: International Universities Press, Incorporated, 1955. $7.50.

The Hospitals Year Book: An annual record of the hospitals of Great Britain and Northern Ireland, incorporating "Burdett's Hospitals and Charities," founded 1889: 1955-56. Edited by J. F. Milne, M.C., B.Sc. (Econ.); and S. R. Speller, LL.B., advisory editor. 8°, cloth, 1116 pp. London: Institute of Hospital Administrators, 1955.

From Witchcraft to Antisepsis: A study in antithesis. By Douglas Guthrie, M.D., F.R.C.S., lecturer on the history of medicine, University of Edinburgh. 8°, cloth, 53 pp. Lawrence, Kansas: University of Kansas Press, 1955. $1.50. (Fifth series, *Logan Clendening Lectures on the History and Philosophy of Medicine.)*

Obstetrical Anesthesia: Its principles and practice. By Bert B. Hershenson, M.D., director of anesthesia, Boston Lying-in Hospital, and clinical associate in anesthesia, Harvard Medical School. With a foreword by Frederick C. Irving, M.D., William Lambert Richardson Professor of Obstetrics, emeritus, Harvard University. 8°, cloth, 403 pp., with 50 illustrations and 17 tables. Springfield, Illinois: Charles C Thomas, 1955. $9.50.

The Pediatric Years: A guide in pediatrics for workers in health, education and welfare. By Louis Spekter, M.P.H., M.D., director, Bureau of Maternal and Child Hygiene, Connecticut State Department of Health. 8°, cloth, 734 pp., with 20 illustrations and 10 tables. Springfield, Illinois: Charles C Thomas, 1955. $12.50.

The Thyroid: A fundamental and clinical text. Edited by Sidney C. Werner, M.D., Sc.D. (Med.). With sixty contributors. 8°, cloth, 789 pp., with 130 illustrations and 65 tables. New York: Paul B. Hoeber, Incorporated, 1955. $20.00.

Pathology Seminars. By Lauren V. Ackerman, M.D.; Arthur C. Allen, M.D.; Colonel J. E. Ash, M.C.; Arthur Purdy Stout, M.D.; and Rupert A. Willis, M.D. Edited by Robert S. Haukohl, M.S., M.D., assistant professor of pathology, Marquette University School of Medicine, and pathologist, Deaconess Hospital, Milwaukee, Wisconsin; and W. A. D. Anderson, M.A., M.D., professor of pathology and chairman of the Department of Pathology, University of Miami School of Medicine, and director of the Pathology Laboratories, Jackson Memorial Hospital, Miami, Florida. 4°, cloth, 195 pp., with 131 illustrations. St. Louis: The C. V. Mosby Company, 1955. $10.00.

Cardiac Diagnosis: A physiologic approach. By Robert F. Rushmer, M.D., associate professor of physiology and biophysics, University of Washington Medical School. 4°, cloth, 447 pp., with illustrations. Philadelphia: W. B. Saunders Company, 1955. $11.50.

The Dynamic Equilibrium of Body Proteins: Hemoglobin, plasma proteins, organ and tissue proteins. By George H. Whipple, M.D., professor of pathology, emeritus, and dean of the School of Medicine and Dentistry, emeritus, University of Rochester, New York. 8°, cloth, 68 pp., with 12 illustrations and 14 tables. Springfield, Illinois: Charles C Thomas, 1956. $3.25.

The Year Book of Radiology: 1955-1956 Year Book Series. Edited by John Floyd Holt, M.D., professor, Department of Radiology, University of Michigan Medical School; Fred Jenner Hodges, M.D., professor and chairman, Department of Radiology, University of Michigan Medical School; Harold W. Jacox, M.D., professor of radiology, Columbia University College of Physicians and Surgeons, and chief, Radiation Therapy Division, Radiologic Service, Presbyterian Hospital, New York City; and Morton M. Kligerman, M.D., associate professor of radiology, Columbia University College of Physicians and Surgeons, and assistant radiologist, Presbyterian Hospital, New York City. 8°, cloth, 413 pp., with 344 illustrations and tables. Chicago: Year Book Publishers, Incorporated, 1955. $9.00.

The Role of Algae and Plankton in Medicine. By Morton Schwimmer, M.D., clinical assistant in medicine, New York Medical College, Metropolitan Medical Center; and David Schwimmer, M.D., assistant professor of medicine, New York Medical College, Metropolitan Medical Center. 8°, cloth, 85 pp., with 9 tables. New York: Grune and Stratton, 1955. $3.-.

Brain Mechanisms and Consciousness: A symposium organized by the Council for International Organizations of Medical Sciences: Established under the joint auspices of UNESCO and WHO. Editor for the Council, J. F. Delafresnaye, C.I.O.M.S., Paris, France. Consulting editors, Edgar D. Adrian (United Kingdom), Frederic Bremer (Belgium) and Herbert H. Jasper (Canada). 8°, cloth, 556 pp., with illustrations and tables. Springfield, Illinois: Charles C Thomas, 1955. $8.50.

Integrated Gynecology: Principles and Practice. In 3 volumes. By I. C. Rubin, M.D.; and Josef Novak, M.D., professor of obstetrics and gynecology, University of Vienna. 8°, cloth, 1869 pp., with 511 illustrations. New York: The Blakiston Division, McGraw-Hill Book Company, Incorporated, 1956. $60.00.

Chemistry and Human Health. By Burnham S. Walker, M.D., Ph.D., professor of biochemistry, Boston University School of Medicine; Isaac Asimov, Ph.D., associate professor of biochemistry, Boston University School of Medicine; and M. Kolaya Nicholas, R.N., M.A., instructor in chemistry and pharmacology, Medical Center, Jersey City Hospital School of Nursing. 8°, cloth, 445 pp., with 10 illustrations, 47 tables and 243 formulas. New York: The Blakiston Division, McGraw-Hill Book Company, Incorporated, 1956. $5.75.

The Biliary Tract: With special reference to the common bile duct. By Julian A. Sterling, M.D., Sc.D., staff surgeon, Albert Einstein Medical Center and Graduate Hospital, chief surgeon, Psychiatric Hospital, and associate in surgery, Graduate School of Medicine, University of Pennsylvania. 8°, cloth, 424 pp., with 94 illustrations, 19 tables and a frontispiece. Baltimore: The Williams and Wilkins Company, 1955. $10.00.

Control of Insect Vectors in International Air Traffic: A survey of existing legislation. 8°, paper, 60 pp. Geneva: World Health Organization, 1955. Price 3/6d., Sw. fr. 2.-, $0.70. Also available in French. (Distributed by Columbia University Press, New York City.)

The Cytology and Life-History of Bacteria. By K. A. Bisset, D.Sc., reader in systematic bacteriology, University of Birmingham. Second edition. 8°, cloth, 164 pp., with 68 illustrations. Baltimore: The Williams and Wilkins Company, 1955. $6.00.

Vascular Surgery. Edited by Daniel C. Elkin, M.D.; and Michael E. DeBakey, M.D. 4°, cloth, 465 pp., with 56 illustrations, 52 tables and 30 charts. Washington, D.C.: Office of the Surgeon General, Department of the Army, 1955. $4.25. (Medical Department, United States Army. *Surgery in World War II.*)

Chest X-Ray Diagnosis. By Max Ritvo, M.D., assistant clinical professor of radiology, Harvard Medical School, instructor in radiology, Tufts University School of Medicine, lecturer on radiology, Boston University School of Medicine, roentgenologist-in-chief and director, Department of Radiology, Boston City Hospital, associate radiologist, Beth Israel Hospital, Boston, and radiologist, Memorial Hospital, Roxbury, Massachusetts, and New England Sinai Hospital for Diseases of the Chest. Second edition, thoroughly revised. 4°, 640 pp., with 633 illustrations and 1 plate. Philadelphia: Lea and Febiger, 1956. $16.00.

Poliomyelitis: Papers and discussions presented at the third international poliomyelitis conference. Compiled and edited for the International Poliomyelitis Congress. 4°, cloth, 567 pp., with 442 illustrations and 82 tables. Philadelphia: J. B. Lippincott Company, 1955. $7.50.

The Interpretation of the Unipolar Electrocardiogram. By Gordon B. Myers, M.D., professor of medicine, Wayne University College of Medicine, and head, Department of Medicine, City of Detroit Receiving Hospital. 4°, paper, 164 pp., with 19 illustrations. St. Louis: The C. V. Mosby Company, 1956. $4.75.

A. M. A. Scientific Exhibits, 1955. Sponsored by Council on Scientific Assembly, American Medical Association. 4°, cloth, 784 pp., with illustrations and charts. New York: Grune and Stratton, 1955. $20.00.

Das kleine Frauenbuch. By Heinrich Martius. 8°, paper, 76 pp., with 51 illustrations by Käthe Droysen. Stuttgart: Georg Thieme, 1956. DM 6.90.-$1.65. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

Arthroplasty. By St. J. D. Buxton, M.B., B.S., F.R.C.S., consulting orthopedic surgeon, King's College Hospital, emeritus lecturer in orthopedics, King's College Hospital Medical School, and consulting orthopedic surgeon to the Army and orthopedic surgeon to Queen Mary's Hospital, Roehampton, and the Royal Masonic Hospital, London. 8°, cloth, 126 pp., with 43 illustrations, 2 plates and a frontispiece. Philadelphia: J. B. Lippincott Company, 1955. $6.00.

The American Drug Index. By Charles O. Wilson, Ph.D., professor of pharmaceutical chemistry, College of Pharmacy, University of Texas; and Tony Everett Jones, M.S., instructor in pharmaceutical chemistry, College of Pharmacy, University of Colorado, and director of pharmaceutical research, Carbisulphoil Company. 8°, cloth, 576 pp. Philadelphia: J. B. Lippincott Company, 1956. $5.00.

Psychological Medicine: A short introduction to psychiatry. By Desmond Curran, M.B., F.R.C.P., D.P.M., senior con-

sultant psychiatrist, St. George's Hospital, and civil consultant in psychologic medicine to the Royal Navy; and Maurice Partridge, M.A., D.M., D.P.M., consultant psychiatrist, St. George's Hospital. Fourth edition. 8°, cloth, 407 pp., with 20 illustrations. Edinburgh: E. and S. Livingstone, Limited, 1955. $5.00. (Distributed by the Williams and Wilkins Company, Baltimore.)

An Elementary Textbook of Psychoanalysis. By Charles Brenner, M.D., lecturer, New York Psychoanalytic Institute, and associate clinical professor of psychiatry, Yale University School of Medicine. 8°, cloth, 219 pp. New York: International Universities Press, Incorporated, 1955. $4.00.

Special Education for the Exceptional. Vol. 1. *Introduction and Problems.* Edited by Merle E. Frampton and Elena D. Gall. Vol. 1. 8°, cloth, 453 pp., with illustrations and tables. Boston: Porter Sargent, 1955. $5.50. Vol. 2. *The Physically Handicapped and Special Health Problems.* 8°, cloth, 677 pp., with illustrations and tables. Boston: Porter Sargent, 1955. $5.50. Vol. 3. *Mental and Emotional Deviates and Special Problems.* 8°, cloth, 700 pp., with illustrations and tables. Boston: Porter Sargent, 1956. $5.50.

Planning Florida's Health Leadership: Medical education in the University. Vol. 5. Edited by Louis J. Maloof. 8°, paper, 161 pp. Gainesville: University of Florida Press, 1955. $1.50. *(Medical Center Study Series.)*

Community Programs for Mental Health: Theory, practice, evaluation. Edited by Ruth Kotinsky and Helen L. Witmer. 8°, cloth, 362 pp. Cambridge, Massachusetts: Harvard University Press, 1955. $5.00. (Published for the Commonwealth Fund.)

Structure of the Ego: An anatomic and physiologic interpretation of the psyche: Based on the psychology of Otto Rank. By Lovell Langstroth, M.D. 8°, cloth, 149 pp., with 11 illustrations. Stanford, California: Stanford University Press, 1955. $4.00.

Operative Technic in General Surgery. Edited by Warren H. Cole, M.D., professor of surgery and head, Department of Surgery, University of Illinois College of Medicine, and chief surgeon, Illinois Research and Educational Hospitals, Chicago. With an introduction by Frank H. Lahey. Second edition. 8°, cloth, 973 pp., with illustrations. New York: Appleton-Century-Crofts, Incorporated, 1955. $20.00.

An Introduction to Psychiatry. By Max Valentine, M.D., D.P.M., senior lecturer. Department of Mental Health, University of Aberdeen, and honorary consultant, Aberdeen Teaching Hospitals. 12°, paper, 300 pp., with illustrations. Edinburgh: E. and S. Livingstone, Limited, 1955. $3.75. (Distributed in the United States by Williams and Wilkins, Baltimore.)

Clinical Analgetics. By E. G. Gross, Ph.D., M.D., professor of pharmacology and head, Department of Pharmacology, State University of Iowa College of Medicine; and M.J. Schiffrin, Ph.D., assistant director of clinical research, Hoffmann-LaRoche, Incorporated, Nutley, New Jersey. 8°, paper, 101 pp., with 3 tables. Springfield, Illinois: Charles C Thomas, 1955. $3.00. (Publication No. 273, *American Lecture Series.)*

Atomic Energy Research at Harwell. By K. E. B. Jay. 8°, cloth, 144 pp., with 9 illustrations and 19 plates. New York: Philosophical Library, 1955. $4.75.

Problems in Amoebiasis. By Charles William Rees, Ph.D., head, Section on Protozoal Diseases, Laboratory of Tropical Diseases, National Microbiological Institute, National Institutes of Health, United States Public Health Service, Bethesda, Maryland. 8°, cloth, 119 pp., with 18 illustrations, 2 tables and a frontispiece. Springfield, Illinois: Charles C Thomas, 1955. $4.75.

The Diagnosis and Treatment of Haemophilia and Its Related Conditions. By R. G. Macfarlane and Rosemary Biggs. 8°, paper, 23 pp., with 2 illustrations and 3 tables. London: Her Majesty's Stationery Office, 1955. 2s. 6d. net. $0.45. *(Medical Research Council Memorandum No. 32.)* (Privy Council.)

New Concepts in Surgery of the Vascular System. By Emile Holman, M.D., professor of surgery, Stanford University School of Medicine, San Francisco. *A. The Immediate and Late Treatment of Arterial Injuries.* (Presented as the David W. Yandell Lecture before the Louisville Surgical Society, Louisville, Kentucky.) *B. The Pathologic Physiology of Poststenotic Dilatation. Its Significance in the Development of Arterial Aneurysms.* (Presented as the Arthur Dean Bevan Lecture before the Chicago Surgical Society, Chicago, Illinois.) 8°, paper, 108 pp., with 47 illustrations and 12 tables. Springfield, Illinois: Charles C Thomas, 1955. $3.50. (Publication No. 271, *American Lecture Series.)*

The Interpretation of Nature and the Psyche. Synchronicity: An acausal connecting principle. By C. G. Jung. *The Influence of Archetypal Ideas on the Scientific Theories of Kepler.* By W. Pauli. 8°, cloth, 247 pp., with illustrations, tables and plates. New York: Pantheon Books Incorporated, 1955. (Sponsored by Bollingen Foundation. No. 51.) $3.00.

NONCLINICAL NOTES

BERTNER FOUNDATION AWARD

Dr. Joseph C. Aub, professor of medical research, Harvard Medical School, and director of medical laboratories at the Collis P. Huntington Memorial Hospital, was presented the Bertner Foundation Award and delivered the Bertner Lecture on March 30 at the Tenth Annual Symposium on Fundamental Cancer Research of the University of Texas M. D. Anderson Hospital and Tumor Institute. The award was established in 1950 in honor of the late Dr. E. W. Bertner, first acting director of the hospital and institute and first president of the Texas Medical Center.

NOTICES

ANNOUNCEMENT

Dr. Phyllis MacNeil announces the opening of her office at 350 Beacon Street, Boston 18, Massachusetts, for the practice of general surgery.

BOSTON CITY HOSPITAL HOUSE OFFICERS' ASSOCIATION

The House Officers' Association of the Boston City Hospital announces the schedule of the remaining evening lecture series to be held in the New Cheever Amphitheater, Dowling Building, Boston City Hospital, at 7 p.m. The program is as follows:

April 17. Sodium Chloride and Hypertension: Some experimental aspects. Dr. John B. Youmans, Vanderbilt University School of Medicine.

April 24. Clinical and Experimental Observations of Host-Parasite Relations in Viral Infection. Dr. Louis Weinstein, Massachusetts Memorial Hospitals — Haynes Department of Infectious Diseases.

May 3. Recent Setbacks in Medicine. Dr. William B. Bean, University of Iowa School of Medicine.

LECTURES ON RADIOBIOLOGY

Dr. Friedrich P. Ellinger will deliver the following lectures on radiobiology at the Massachusetts Institute of Technology and the Massachusetts General Hospital:

April 25, at 7 p.m. Fundamental Biology of Ionizing Radiation. Room 10-275, Massachusetts Institute of Technology.

April 26, at 4:30 p.m. Radiation Hazards. Outpatient Lower Amphitheater, Massachusetts General Hospital.

April 27, at 4:30 p.m. Newer Concepts of Radiation Illness and Its Treatment. Outpatient Lower Amphitheater, Massachusetts General Hospital.

All interested physicians and scientists are invited to attend.

AMERICAN COLLEGE OF CHEST PHYSICIANS AND THE OVERHOLT THORACIC CLINIC

There will be a combined meeting of the New England States Chapter of the American College of Chest Physicians and the Overholt Thoracic Clinic in the Joslin Auditorium of the New England Deaconess Hospital, Boston, on Wednesday, April 18, at 4 p.m.

Drs. Julia G. Arrowood, Ernest Sneddon and Leroy D. Vandam will present a symposium on anesthesia in thoracic surgery.

GUILD OF PRESCRIPTION OPTICIANS OF AMERICA

The Guild of Prescription Opticians of America announces that eighteen fellowships in ophthalmology will be established over the next three years. The fellowships are provided on a regional basis, with the United States and Canada divided into six geographic areas, each having approximately the same number of three-year ophthalmology residencies available. The Committee of Ophthalmology will select a recipient in each area. The first fellowship in each of the six areas will be initiated this year, the second one next year, and the third one in the following year. Thereafter, as each three-year residency is completed, a new fellowship will become available, constantly maintaining the number at eighteen. A stipend of $1,800, payable in monthly installments, will be awarded over the three-year period of residency. Further information may be obtained from the Guild of Prescription Opticians of America, Inc., 110 East 23rd Street, New York 10, New York.

SOCIETY MEETINGS AND CONFERENCES

APRIL 15–20. American College of Allergists. Page 399, issue of February 23.
APRIL 16. Hartford Medical Society. Page 242, issue of February 2.
APRIL 16–18. Aero Medical Association. Page 585, issue of March 22.
APRIL 16–21. American Academy of Pediatrics. Page 399, issue of February 23.
APRIL 17. South End Medical Club. Page 676, issue of April 5.
APRIL 17, 24 and MAY 3. Boston City Hospital House Officers' Association. Page 725.
APRIL 18. Greater Boston Medical Society. Page 208, issue of August 4.
APRIL 18. Third Annual Surgical Seminar. Page 676, issue of April 5.
APRIL 18. American College of Chest Physicians and the Overholt Thoracic Clinic. Notice above.
APRIL 22. Massachusetts Chapter, American Academy of General Practice. Page 676, issue of April 5.
APRIL 23–26. International Academy of Proctology. Page 399, issue of February 23.
APRIL 25. Soldiers Home, Chelsea. Page 676, issue of April 5.
APRIL 25–27. Lectures on Radiobiology. Notice above.
APRIL 26. Phi Delta Epsilon Fraternity Graduate Club Program. Page 118, issue of July 21.
MAY 1–5. Sixth National Congress on Pediatrics. Page 491, issue of March 8.
MAY 2. Postgraduate Medical Institute. Page 487, issue of September 15.
MAY 3–5. American Goiter Association. Page 348, issue of August 25.
MAY 14–18. American Nurses' Association. Page 491, issue of March 8.
MAY 22–24. Massachusetts Medical Society Annual Meeting.
MAY 28–JUNE 1. European Symposium on Vitamin B. Page 578, issue of September 29.
JUNE 1–9. International Medical-Surgical Meetings. Page 540, issue of March 15.
JUNE 4–13. Army Medical Service Postgraduate Course. Page 84, issue of July 14.
JUNE 21–23. Society of Nuclear Medicine. Page 1092, issue of December 15.
JUNE 21–24. American Academy of Dental Medicine. Page 944, issue of December 1.
AUGUST 19–23. American College of Chest Physicians. Page 840, issue of November 10.
SEPTEMBER 3–5. Congress on Blood Transfusion, Blood Banks and Hematology. Page 297, issue of February 9.
SEPTEMBER 10–14. American Dietetic Association. Page 1180, issue of December 29.

CALENDAR FOR THE WEEK BEGINNING THURSDAY, APRIL 19

THURSDAY, APRIL 19
Holiday

FRIDAY, APRIL 20
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m. Pediatric Grand Rounds. Thorndike Amphitheater, Boston City Hospital.
*1:00–3:00 p.m. Combined Medical-Surgical Grand Rounds. Stearns Auditorium, New England Center Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*2:00–3:00 p.m. Pathology Conference. Dr. James Graham. Saint Elizabeth's Hospital.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Morton Street, Jamaica Plain.
*4:30 p.m. Neuroradiologic Conference. X-Ray Conference Room, New England Deaconess Hospital.

SATURDAY, APRIL 21
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:30–10:00 a.m. Surgical Grand Rounds. Drs. Charles G. Child, III, A. J. A. Campbell and staff. First (Tufts) Surgical Service, New Cheever Amphitheater, Dowling Building, Boston City Hospital.
*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*9:30–11:00 a.m. Surgical House Officers' Conference. Second-Floor Conference Room, Carney Hospital, Dorchester.
*10:30 a.m. Teaching Ward Rounds. Ward South 2, Free Hospital for Women.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Hematology Conference (Blood Clinic). Dr. William Dameshek. Stearns Auditorium, New England Center Hospital.

MONDAY, APRIL 23
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:30–9:30 a.m. Clinic by Entire Surgical Staff and Anesthesia Staff. New Cheever Amphitheater, Dowling Building, Boston City Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:30 p.m. Staff Conference. Child Psychiatry. By appointment. Conference Room (Burnham 7), Massachusetts General Hospital.
*12:00 m.–1:00 p.m. Medical-Pathological Conference. Stearns Auditorium, New England Center Hospital.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*2:00–3:00 p.m. X-Ray Conference. Dr. William Carey. Saint Elizabeth's Hospital.
*3:00–4:00 p.m. Neuroradiologic Conference. Stearns Auditorium, New England Medical Center.
*4:00 p.m. Clinicopathological Conference. Pathology Conference Room, Beth Israel Hospital.
*4:00–5:30 p.m. Anesthesiology Conference. The Analeptics. Dr. Lipschitz. Surgical Conference Room, Peter Bent Brigham Hospital.
*5:00–6:30 p.m. Anesthesia Group of the Lahey Clinic. Joslin Auditorium, New England Deaconess Hospital.

(Concluded on page xxxii)